BRAIN

A JOURNAL OF NEUROLOGY

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A Journal of Neurology

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VOLUME LXXIII

MACMILLAN & CO., LIMITED
ST. MARTIN'S STREET, LONDON
NEW YORK: THE MACMILLAN COMPANY
1950

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CONTENTS

	PAGE
Functional Capacity of the Isolated Human Spinal Cord. Robert A. Kuhn	1
Lead in Relation to Disseminated Sclerosis. A. M. G. Campbell, G. Herdan, W. F. T. Tatlow and E. G. Whittle	52
The Lumbar Cerebrospinal Fluid Protein in Intracranial Meningiomas. W. Eugene Stern	72
Non-penetrating Injuries of the Median Nerve at the Wrist. David Kendall	84
The Human Pyramidal Tract. XVIII: An Analysis of Its Pathophysiological Status. A. M. Lassek	95
Survival in Disseminated Sclerosis: A Clinical Study of a Series of Cases First Seen Twenty Years Ago. R. S. Allison	103
Thresholds of Cortical Representation. E. G. T. Liddell and C. G. Phillips ...	125
Encephalitis and Encephalomyelitis in England and Wales During the Last Decade. J. G. Greenfield	141
Visual-Spatial Agnosia Associated with Lesions of the Right Cerebral Hemisphere. J. McFie, M. F. Piercy and O. L. Zangwill	167
Cortical Rhythms Not Seen in the Electroencephalogram. Denis Williams and Gerald Parsons-Smith	191
A Case of Auditory Agnosia. Margaret Reinhold.	203
Sensory Changes in Procaine Nerve Block. D. C. Sinclair and J. R. Hinshaw	224
The Chemistry of Cerebral Cysts. J. N. Cumings	244
The Advance of Functional Recovery after Radial Nerve Lesions in Man. R. E. M. Bowden and D. A. Sholl	251
The Validity of the Concept of Multiplicity of Representation in the Motor Cortex under Conditions of Threshold Stimulation. E. Gellhorn ...	267
The Specificity of the Electromyographic Method for the Investigation of the Motor Cortex. E. Gellhorn and D. A. Johnson	275
Adult Toxoplasmosis in One Family. A. M. G. Campbell and F. Clifton ...	281
Late Infantile Metachromatic Leuco-Encephalopathy, with Primary Degeneration of the Interfascicular Oligodendroglia. W. Russell Brain and J. G. Greenfield	291
Myotonia Congenita, Dystrophia Myotonica and Paramyotonia: Reaffirmation of their Identity. Otto Maas and A. Spencer Paterson	318
The Effect of Head Posture on the Manometrics of the Cerebrospinal Fluid in Cervical Lesions: A New Diagnostic Test. Lawrence Kaplan and Foster Kennedy	337
Anterolateral Cordotomy: Results, Complications and Causes of Failure. James C. White, William H. Sweet, Ralph Hawkins and Richard G. Nilges	346
The Origin, Course and Termination of the Prefronto-Pontine Tract in the Human Brain. Elisabeth Beck	368

U of M Bindery JAN 19 '56

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Electroencephalogram in Subacute Progressive Encephalitis. William Cobb and Denis Hill 392

Basilar Impression of the Skull. J. E. A. O'Connell and J. W. Aldren Turner 405

Blood Pyruvate Estimations in the Diagnosis and Treatment of Polyneuritis. C. L. Joiner, B. McArdle and R. H. S. Thompson 431

Fits of Laughter (Sham Mirth) in Organic Cerebral Disease. J. Purdon Martin 453

The Cerebral Basis of Consciousness. W. Russell Brain 465

A Comparison of the Sensory Dissociation Produced by Procaine and by Limb Compression. D. C. Sinclair and J. R. Hinshaw 480

Symptomatic "Cataplexy" or Chalastic Fits in Cortical Lesion of the Frontal Lobe. Sven Ethelberg 499

Further Studies on the Role of Proprioception in Cortically Induced Movements of the Foreleg in the Monkey. E. Gellhorn and D. A. Johnson 513

A Study of Retrograde Degeneration in the Oculomotor Nucleus of the Rhesus Monkey, with a Note on a Method of Recording Its Distribution. R. Warwick 532

Notices of Recent Publications 121, 280, 427, 544

MARCH, 1950

BRAIN

VOL. 73, PART 1.

FUNCTIONAL CAPACITY OF THE ISOLATED HUMAN SPINAL CORD

BY

ROBERT A. KUHN[1]

I. INTRODUCTION

THE recent world conflict with its many casualties from high-velocity missiles resulted in large numbers of patients with spinal cord injuries. Rapid, efficient evacuation and many improved techniques in treatment greatly increased survival rates in these men. Coincidentally, an opportunity was provided for the study of unprecedented numbers of men with partial or complete lesions of the spinal cord.

In a recent paper Kuhn and Macht (1949) drew attention to the involuntary activity patterns manifested by skeletal muscles innervated by the isolated portion of the cord in surgically verified cases of complete cord transection. The most typical sequence of reflex activity following severance of the spinal cord in this series of patients was: (1) Spinal shock (total flaccidity); (2) minimal reflex activity; (3) flexor spasms; (4) alternating flexor and extensor spasms; and (5) predominant extensor spasms. In addition it was noted that sustained quadriceps and ankle clonus, extensor thrust, and spinal standing may occur in spinal men—observations which were at variance with those of earlier observers. It seems certain that many of the discrepancies between these findings and those of earlier investigators can be explained by the greater duration of life and, secondarily, by the better physical condition of spinal men studied in recent years.

II. MATERIAL STUDIED

In an attempt to estimate the functional capacity of the chronically-isolated human cord, a study was made of reflex patterns elicitable below the level of cord transection. The present report is based on data obtained at Cushing Hospital, Framingham, Mass., during the years 1946-1947. Twenty-nine individuals with total transection of the cord were studied. In every case the completeness of the transection was ascertained by exploratory laminectomy at the site of injury. Levels of transection ranged from D-2 to D-12, and in 27 men the injury had occurred two or

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more years prior to the periods of examination. Each patient was subjected to neurologic examination at frequent intervals. With one exception (A. S.), all of these men are alive, and most are in excellent physical condition at the present date. The extreme reflex activity manifested by many patients has been permanently abolished by anterior dorsolumbar rhizotomy.

III. Spinal Shock

Spinal shock, defined here as that state of total abolition of all tendon reflexes and profound depression of other reflex activity below the level of cord transection which immediately follows such a lesion, occurs frequently—probably always—in men. In general, minimal reflex activity appears within a period of one to six weeks, to be followed by stages of flexor spasms, alternating flexor and extensor spasms, and, eventually, predominant extensor spasms. The records of each of the men in this series invariably stated that a period of complete flaccidity immediately followed division of the cord. Though these records were not sufficiently detailed to establish that there had been a total areflexia, they did indicate at least a profound depression of reflexes below the severed cord.

Two patients sustaining recent transection of the cord were studied from the day of injury and for approximately seven months thereafter. The course in both was marked by an initial complete areflexia below the level of cord division. In one man, priapism and transient toe movements constituted the sole evidence of early reflex activity, whereas weak flexor and extensor movements of the toes appeared simultaneously with anal and bulbocavernosus reflexes in the second. The following excerpts were taken from the protocols of these subjects:

C. S., aged 19, was thrown from a motor-cycle August 1, 1947, sustaining immediate, complete sensory and motor paralysis below the costal margins. On admission to the hospital a few hours later, examination disclosed priapism, a sensory level at the D–6 segment, absent deep and superficial reflexes, and minimal flexion movements of the toes. Within forty-eight hours the toe movements disappeared. On the third day an anal reflex was elicited, and this response was maintained thereafter. In addition, an incomplete penile erection resulted during cleansing of the perineum and genitals. Detailed daily examinations revealed no further changes until nineteen days after injury, when tremulous, quivering movements of the toes occurred in response to plantar stimulation. The following day, swabbing of the penis evoked a complete erection for the first time. Reflex flexor muscle activity in the lower limbs increased steadily during the succeeding weeks.

S. B., aged 29, was injured September 28, 1947, sustaining immediate, complete paralysis below the nipples. Initial examination disclosed complete areflexia, with sensory and motor loss below the fourth dorsal segment. There was no priapism. His neurological status remained unchanged during succeeding weeks. Twenty-four days after injury, however, examination revealed for the first time slight quivering flexor and extensor movements of the hallux and toes. Weak bulbocavernosus and anal reflexes could be elicited the same day. Activity in skeletal musculature below the level of cord division spread slowly during succeeding weeks, and a fairly well-executed response of triple flexion was evocable at the end of the second month after injury.

Each of these subjects received excellent early care, and both remained free from febrile illnesses throughout a seven-month period of observation. Their earliest reflex manifestations appeared after nearly equal intervals following cord injury, if the initial, evanescent plantar responses in C. S. are ignored.

Judgment as to the duration of spinal shock in patients with long-sustained division of the cord was difficult since, except for 4 men, the records were not sufficiently descriptive to ascertain the period of total areflexia. It is apparent that even these 4 subjects (Table I) had progressed beyond the stage of spinal shock at the time of their detailed examinations. Thus, J. D. displayed by this time minimal reflex activity, and the others were probably well beyond this stage. Judging by the type of activity manifested by these men, each had emerged from spinal shock within a maximum of two weeks after transection of the cord. Evidence relating to duration of spinal shock obtained from patients was not reliable. Estimates by all subjects of the lapse of time preceding initial reflex movements ranged between 20 and 255 days after injury, and were in reality a rough measure of the number of days preceding the first gross movements in the lower extremities.

TABLE I.—INITIAL ACTIVITY (DAYS) AFTER INJURY

Patient	*Estimate by patient*	*Actual*	*Type of activity*
J. D.	180	14	Bilateral Babinski signs
R. S.	49	19	Bilateral knee and ankle jerks
G. G.	21	36	Bilateral knee-jerks
P. C.	21	48	Active reflex withdrawal of both lower extremities

IV. LONG-SUSTAINED AREFLEXIA BELOW CORD TRANSECTION

Five of the 29 subjects studied had, apparently, remained in a state of complete flaccidity below the level of cord transection since the day of injury (Table II). There was striking similarity between patients, with the exception of E. G., who manifested unmistakable evidences of function in the sacral segments subserving activity in the bladder and in the vesical and rectal sphincters. A case report of a typical representative of this group, and of E. G., who differed significantly in his neurologic status, follows :

TABLE II.—DATA ON 5 PATIENTS WITH TRANSECTION OF THE CORD, AND CHRONIC FLACCIDITY BELOW THE LEVEL OF INJURY

Patient	*Segmental level*	*Days since injury*	*Muscular configuration*	*Cutaneous and tendon reflexes*	*Bladder status*	*Genital reflexes*	*Skeletal musculature*
R. P.	D–6	1,102	Marked atrophy	Absent	Atonic	Absent	Flaccid
A. S.	D–3	1,225	Extreme atrophy	Absent	Atonic	Absent	Flaccid
J. T.	D–8	1,098	Extreme atrophy	Absent	Atonic	Absent	Flaccid
T. M.	D–5	736	Extreme atrophy	Absent	Atonic	Absent	Flaccid
E. G.	D–8	1,283	Marked atrophy	Anal reflex	Reflex	Present	Fibrillary (?) movements

Case 1.—*Complete areflexia below the level of cord transection three years after injury.*

J. T., aged 29, was injured by a shell fragment on September 27, 1944. Immediate, complete sensory and motor paralysis resulted below the level of the nipples. X-ray examination revealed comminuted fractures of the fifth and sixth dorsal vertebræ. Cutaneous sensory loss was complete below D–2 at initial examination. Exploratory laminectomy on December 3, 1946, disclosed a gap of 3 cm. between the ends of the spinal cord at the level of the D–3 vertebra.

The following examination was conducted three years after injury.

Physical appearance.—The patient is examined lying supine. There is an indwelling urethral catheter ; rectal temperature is normal ; two rather small (3 cm.) decubitus ulcers overlie the right greater trochanter and the lower sacrum, respectively. There is extreme emaciation below the level of cord lesion. The iliac crests are symmetrically prominent, and the muscles of the buttocks, thighs, and legs are severely atrophied. The lower limbs lie flat and slightly rotated externally at the hips, with the feet in limp hyperextension. Anteriorly and posteriorly there is a band of cutaneous hyperæsthesia at the D–5 dermatome, and complete cutaneous sensory loss below that area.

Reflex activity.—There is no apparent reflex response to a variety of stimuli applied below the level of cord division. Tendon and cutaneous reflexes are completely absent. There is hypermobility of all joints of the flaccid lower extremities. The anal sphincter is patulous and the prostate very small and soft. The only activity noted in this patient is a delayed penile shrinking following the application of pin-prick to that organ.

Comment.—This patient is a typical representative of the small group of men who had never developed reflex muscle activity below the level of cord lesion. In addition to complete lack of reflex bowel control, this man possessed an atonic bladder and had, characteristically, failed to develop reflex penile erections following injury. The extreme emaciation of his paralysed body was typical of that shown by other and similarly flaccid and areflexic patients. Decubitus ulcers, when they appeared in such men, were particularly recalcitrant to therapeutic measures.

Case 2.—*Minimal reflex activity below the level of cord transection three years after injury. Skeletal muscle movements in the lower limbs.*

E. G., aged 32, sustained a gunshot wound March 26, 1945, and immediately lost all sensation and motion below the costal margins. X-ray films showed comminuted fractures of the fifth and sixth dorsal vertebræ. Initial examination revealed a wide band of cutaneous hyperæsthesia below the costal margins, with complete anæsthesia distally. A laminectomy performed a month after injury, disclosed complete transection of the cord at the level of the D–7—D–8 vertebral interspace.

Physical appearance.—The patient is examined lying supine. Rectal temperature is normal and the patient is catheter-free. There are no decubiti. Muscle atrophy is generalized and marked below the level of cord lesion. The lower limbs lie flaccid and rotated slightly externally at the hips. Cutaneous sensation is normal to the level of the D–7 dermatome, but totally absent below that segment.

Interim note.—Skeletal muscle activity in the lower limbs was completely absent for three years after division of the cord. The patient then first noted fine, barely perceptible " quiverings " in his anterior thigh musculature. He has been unable to detect any change in the character or intensity of this muscle activity since it was first observed.

Reflex activity.—The lower extremities are hypermobile and completely flaccid. Tendon reflexes are absent, and various intense stimuli evoke no apparent muscle response. Pin-prick within the genital zone elicits the anal reflex, and delayed progressive contraction of the scrotum and penis. Anal sphincter tone is well maintained. Penile erection occurs with gentle friction at the glans.

Though no activity is apparent in the limbs under conditions of ordinary lighting, close inspection of the patient under oblique light reveals an extremely slight but unmistakable " shimmering " movement which involves the greater part of the thigh and leg musculature bilaterally. Nocuous and innocuous stimulation causes no visible or palpable alteration of this skeletal muscle activity.

Comment.—It is possible that this patient had begun to manifest reflex activity in the skeletal musculature innervated by his isolated cord three years after injury. Certain segments of his caudal cord, however, had evidently functioned well since shortly after transection occurred. A fair reflex bladder was established within four months of injury, and, at the same time, the patient noted periodic penile erections. Automatic bowel control was established within six months of severance of the cord. These functions have been well maintained. The patient may be considered, therefore, to have reached the stage of minimal reflex activity in less than six months of his injury. Several drugs failed to influence the described muscle activity in the lower extremities. Thus, aqueous curare administered by the intravenous route to the point of masseter weakness failed to abolish it. The intravenous administration of tetra-ethylammonium chloride (7 mg./Kg.) had likewise no effect, though there was satisfactory blockage of autonomic ganglia, evidenced by a moderate fall in blood pressure, dryness of the mouth, pupillary dilatation, and marked decrease in bladder activity. Finally, 8 c.c. of 1 : 2,000 prostigmine administered parenterally did not modify perceptibly the shimmering movements. The neurologic status of this patient is unique in that, for a period of three and a half years following division of the cord, responses mediated by the isolated segment have not progressed beyond the stage of minimal reflex activity.

It was possible to determine the functional status of the left sciatic nerve in another of these flaccid patients (A. S.) during the course of an ischial flap procedure (Macht and Kuhn, 1948). Faradic and galvanic stimulation of the exposed nerve trunk failed to elicit responses in the musculature of that limb, and direct observation at the operative site disclosed neither the characteristic colour of denervated muscle nor fibrillary movements in the exposed muscle tissue. Direct stimulation of the exposed muscle failed to cause any contraction.

Muscle atrophy was severe to the point of extreme emaciation in 3 of the patients, and in the remaining 2 men it was marked. There was symmetrical involvement of the muscles of the lumbar region, pelvis, and lower limbs. Wasting of the musculature of the legs was obvious in all of these men. Hypermobility of the hip, knee, and ankle joints was characteristic if physiotherapy was maintained. Relaxation of the medial and lateral ligaments of the knee was an especially striking finding. In the supine position, the lower extremities were usually rotated slightly externally at the hips, with the feet in limp, chronic hyperextension. It was of interest that these flaccid patients did not experience spinal sweating. The pilomotor and sudomotor hyperactivity which could be induced in most subjects who exhibited reflex activity in the skeletal musculature below the level of cord transection was completely absent. Bladder over-distension occasionally elicited a complaint of frontal headache and a slight feeling of warmth over the face (A. S.), but the profuse autonomic discharge noted in many other patients was lacking. Gross tests using hot tea and coffee by mouth plus the testimony by

the men that, in a hot environment, they sweated only above the level of their cord lesion, suggested that thermoregulatory sweating was abolished below the region of spinal injury. Despite the conspicuous lack of spinal and thermoregulatory sweating these men, in common with the majority of subjects, stated that there were painful or, frequently, uncomfortable sensations related to posture. Total absence of awareness of bladder distension was a finding in all men of this group. Whereas the bladder of E. G. could empty reflexly at a certain volume, the remaining patients relied entirely on palpation of a sizable suprapubic lump, on "by-the-clock" release of a catheter clamp, or on manual pressure in the suprapubic region. The probability of serious over-distension of the bladder was thus considerably enhanced in four men, since the detrusor failed to contract automatically.

V. Minimal Reflex Activity

The two men (C. S. and S. B.) observed during this stage displayed weak reflex muscle activity of variable pattern in response to nociceptive plantar stimulation. Stimuli of a proprioceptive nature were found to be completely ineffective in the elicitation of reflex activity. Movements were slight and tremulous, and occurred invariably in the distal parts of the lower extremities. Initial activity was never noted to involve muscles of the lumbar region, abdomen, pelvis, or thighs. Tremulous twitching of the toes, brief flexion or extension of the hallux, and slight flexion or extension of the foot were among the earliest evidences of the onset of skeletal muscle activity. Though certain of the minimal responses were initially transient, later the movements became stronger, more easily elicited, and usually included additional and more proximal muscle groups. Quivering side-to-side movements of the toes were observed frequently and did not differ in appearance from similar movements elicited during much later stages. Some subjects evidently pass through this early phase of activity quite rapidly. Thus, patient C. S. was noted to exhibit toe movements within nineteen days of injury, and two weeks later weak flexor responses were palpable in the leg and thigh. Similarly, flexor muscle contraction occurred in the thighs of patient S. B. ten days after the first reflex movements had been observed. In these men, though gross movements of the thighs or legs were not demonstrable at the time, flexor muscle contractions were quite apparent in the musculature of the limbs. Flexor withdrawal, i.e. flexor muscle contraction sufficient to move the limb, occurred at the end of twenty-five days in C. S. and on the 45th day in S. B. Wide variation in the number of days preceding development of well-marked responses seemed to be the rule rather than the exception.

As has been mentioned, bulbocavernosus and anal responses and reflex penile erection were noted early in this stage. Patient C. S. exhibited priapism when examined a few hours after injury and an anal reflex was elicited seventy-two hours after transection of the cord, and was retained

thereafter. Though priapism was not present three days after division of the cord, incomplete penile erection could be evoked reflexly. Approximately two weeks later reflex erections were easily elicited and were then complete. Anal and bulbocavernosus reflexes were not present until twenty-four days after the cord of S. B. had been divided, and then appeared simultaneously with toe movements. Reflex erections at this time were incomplete.

VI. Flexor Activity

It has been suggested elsewhere (Kuhn and Macht, 1949) that flexor responses appear to be early manifestations of the reflex activity exhibited by spinal men, while the extensor movements, if they develop at all, do so invariably at a later date, and then do not lead to abolition of the flexor activity. Flexor activity in the lower extremities of 2 men who were observed from the day of cord transection progressed in a definite sequence, and data available on all other men indicate that a similar sequence occurred in their limbs. As the state of spinal shock lessened, the tremulous toe movements which could initially be elicited changed to a typical Babinski pattern, flexor movements of the foot appeared, and eventually, the knee and the thigh participated in the

Table III.—The Flexor Reflex: Flexor Muscle Responses to Plantar Stimulation

Patient	*Segmental level of lesion*	*Movements of hallux and toes*	*Dorsiflexion of foot*	*Flexion of leg and thigh*	*Abdominal and lumbar responses*
J. Dr.	D–3	Active	Active	Weak	Absent
L. D.	D–9	Active	Active	Active	Absent
M. D.	D–5	Active	Active	Active	Absent
H. F.	D–7	Active	Active	Active	Active
T. McC.	D–4	Absent	Absent	Active	Absent
R. B.	D–4	Absent on left	Absent, left	Weak	Absent
W. M.	D–10	Active	Active	Active	Absent
R. S.	D–2	Active	Weak	Weak	Absent
J. W.	D–9	Active	Active	Active	Absent
J. D.	D–8	Active	Active	Active	Absent
J. Z.	D–3	Active	Active	Incomplete	Ipsilateral lumbar activity
J. B.	D–6	Hallux quiescent	Active	Active	Absent
P. P.	D–5	Active	Active	Active	Ipsilateral lumbar activity
W. D.	D–12	Active	Active	Active	Absent
F. B.	D–10	Active	Active	Active	Absent
D. P.	D–5	Active	Active	Active	Absent
P. C.	D–6	Active	Active	Incomplete	Absent
D. K.	D–2	Hallux quiescent	Active	Incomplete	Absent
V. H.	D–3	Active	Active	Incomplete	Absent
J. V.	D–10	Active	Active	Active	Absent
D. L.	D–9	Toes quiescent	Active	Active	Absent
G. G.	D–8	Active	Active	Active	Absent

steadily strengthening reflex flexion. Extensor activity usually developed only after the paralysed limbs had become capable of responding to an adequate stimulus with a complete response of triple flexion.

A complete flexor response, or some fraction thereof, could be elicited constantly and predictably in each of the 22 men who had survived transection of the cord for long periods, and who manifested reflex activity in the skeletal musculature innervated by the isolated segment (Table III).

A. *Muscles of the Lower Extremities Involved in Reflex Flexion*

A complete triple-flexion response appeared to employ the same flexor muscles as those enumerated by Sherrington (1910) for the spinal cat and dog. In addition, the adductors of the thighs participated in the reaction. Identification of the muscles of the thigh and leg activated in the response was less troublesome if a mild plantar stimulus was employed, for the individual muscle masses could then be singled out. Contraction of the sartorius muscle was especially notable in thin patients, and tightening of this muscle and of the tensor fasciæ latæ was usually palpable in others. Contraction of the medial hamstrings was always easily accessible to palpation. The semimembranosus muscle showed consistently the most powerful reflex response. The belly of this muscle formed a prominent ridge along the medial thigh during withdrawal, and identification was facilitated by following the tendon to its point of insertion. The semitendinosus and gracilis muscles showed much weaker contraction. In most instances it was difficult to determine, either visually or by palpation, whether an increase of tonus or an actual muscle contraction was occurring in the biceps femoris. The rectus femoris was usually quiescent. In an occasional subject, contraction in the biceps or the rectus femoris muscles was unmistakable. The iliopsoas muscle invariably showed strong contraction. The tibialis anterior and extensor hallucis longus demonstrated reflex response in most men. Excluding the flexors and extensors of the hallux and toes, the only muscles noted to contract equally powerfully in flexion and in extension were the adductors of the thigh.

B. *The Form of Reflex Flexion*

Even in the few individuals manifesting extreme flexor activity with minimal plantar stimulation, certain fractions of the maximal reflex response could be isolated under conditions which left little doubt that the remaining flexor musculature did not contract. The muscle contractions resulting from application of nociceptive stimulation to the plantar surfaces of this group of spinal men appeared to be evocable in steps. Muscle contractions were related directly to the level of reflex excitability exhibited by the patient at the time of examination and to the intensity and frequency of the stimuli.

Typical flexion-withdrawal, evoked in response to plantar pin-prick, included the following activities:

(1) *Toe and hallux movements.*—A characteristic response included rapid, marked dorsiflexion and relaxation of the hallux, with simultaneous quivering plantar flexion and fanning of the remaining four toes. By utilizing minimal stimuli it was possible occasionally to elicit the hallux reaction alone, though in most patients hallux and toe movements were simultaneous. If increase of tonus occurred in the hamstrings and the adductors of the thigh, it was not palpable. 10 patients exhibited consistently strong hallux dorsiflexion and simultaneous fanning plantar flexion of the toes; in 4 other individuals the pattern was identical but plantar flexion was unaccompanied by fanning; and in 3 patients, though the hallux remained unresponsive to plantar stimulation, sharp dorsiflexion occurred in the four toes. One man showed dorsiflexion of the hallux but his toes remained immobile, in another all five digits dorsiflexed, and a third demonstrated a typical pattern on the left, but all digits plantar flexed on the right. In one patient with severe extensor activity, no reactions of the hallux or toes could be obtained despite repeated trials, and one man demonstrated plantar flexion of all digits.

The contraction phase of toe and hallux movements appeared to be uniformly abrupt. In most men, contraction and relaxation phases of the movements were quite rapid in response to a brief stimulus, but as the intensity or duration of the latter was increased, relaxation of the hallux was delayed. The protocol of one patient may be referred to as typical:

> The application of a short, moderate stroke or of light pin-prick to the medial plantar surface of the arch elicits a rapid, marked dorsiflexion of the hallux on the ipsilateral side. There is simultaneous plantar flexion and fanning of the toes. Contraction and relaxation of all digits occur over a total time interval of perhaps one second. If the stimulus (stroke) is prolonged two to three seconds, hallux dorsiflexion is maintained accordingly, though its initial height usually decreases. Complete relaxation of the remaining toes to the resting position, though delayed slightly in comparison to relaxation from a brief stimulus, occurs during stimulation, and thus always precedes hallux relaxation by an appreciable time-interval. Complete relaxation of the hallux does not occur until the stimulus is withdrawn.

Frequently a jerking, dysrhythmic series of toe movements was obtained by applying a pin at the heel and drawing it slowly along the length of the plantar surface. The hallux and toes reacted exactly as they would to a series of discrete, irregularly-spaced stimuli. In other patients, particularly those manifesting strong extensor reactions, initial hallux dorsiflexion was fairly well maintained throughout the application of a prolonged, steady moving stimulus (six to ten seconds).

In addition to the several general patterns of flexor activity elicited by plantar stimulation, an occasional subject showed a pattern of local reflex muscle response related to stimulation of specific areas of the sole. In patient V. H., pin-prick applied to the lateral plantar surface elicited consistently a pattern of hallux dorsiflexion, plantar flexion and fanning

of the toes, and eversion of the foot, whereas medial plantar stimulation resulted in similar toe movements with strong inversion and plantar cupping. In the same patient were seen the only crossed movements restricted to the foot and elicited by minimal ipsilateral plantar stimuli. Light pin-prick of one plantar surface was found on repeated testing to induce crossed plantar flexion of all toes, and occasional slight dorsiflexion of the foot.

(2) *Dorsiflexion of the foot.*—In approximately one-half of the patients it was possible, by using varied intensities of stroke and pin-prick on the ball of the foot and medial plantar surface, to obtain fairly marked contraction in the anterior tibial muscle without perceptible or palpable changes in the thigh or pelvic musculature. Flexion of the foot was always accompanied by the toe and hallux movements characteristic for the patient, i.e. dorsiflexion of the foot was an added response. The foot typically gave an abrupt, jerking upward twitch. It rarely showed the sustained flexor activity occasionally manifested by the hallux. Attempts to prolong anterior tibial and peroneal muscle contraction resulted usually in intermittent jerking, or in complete withdrawal of the limb.

(3) *Flexion of leg and thigh.*—When flexor muscle contractions were provoked in the leg and thigh by either innocuous or nocuous plantar stimuli, they ordinarily occurred simultaneously, and it was not possible to detect visually any differences between muscle reaction-times. In the usual subject, response to a moderate plantar pin-prick was withdrawal, of the extremity. The composite reflex reaction was then an abrupt jerking triple-flexion, followed frequently by an equally abrupt relaxation of the entire limb. The reflex response thus resembled closely a muscle twitch in the steepness of the contraction and relaxation phases. Completeness of induced triple-flexion as measured by gross range of movement varied considerably among the patients, but remained relatively constant in a given subject. The total pattern was greatly attenuated in some men, and severe stimulation resulted in barely perceptible gross movements of the extremity, though individual muscle contraction in the thigh, leg, and foot was both visible and palpable. In the majority of the men, a brief plantar pin-prick of moderate severity sufficed to produce partial or complete withdrawal.

The relaxation phase of the flexor response (and in rare instances the phase of flexion) was complicated frequently by the appearance of extensor activity and crossed movements. Crossed flexion of leg or thigh was not observed to follow ipsilateral stimulation of the sole in any patient.

If the response was attenuated and the sole apparent activity consisted of dorsiflexion of the foot, and perhaps of slight flexion of the limb at the knee and hip in addition, the jerking contraction and abrupt relaxation resulted in no significant change in the position of the limb. With more vigorous response of the stimulated extremity and resultant increased flexion at the knee and hip, the falling limb tended to strike on the heel and to slide flat like a dead weight. A minor degree of external rotation

of the thigh was usually apparent with this partial withdrawal. Further accentuation of external rotation resulted when triple-flexion was complete, so that the limb was no longer in a straight line with the trunk but slightly abducted and externally rotated. When withdrawal jerked the thigh beyond a 90 degree angle at the pelvis, the leg became tucked up in a position of acute flexion at the knee, and the heel usually lay beneath the thigh. As relaxation occurred, the lateral plantar surface of the heel acted as a support and pivot for the limp extremity, and the latter thus remained precariously balanced in an abducted and partially-flexed position. Any disturbance of this balance resulted in immediate loose collapse of the extremity to the extended position. Nociceptive stimulation of the plantar surface with the flaccid extremity in the flexed, abducted position rarely elicited gross movements, though slight contraction of the muscles productive of reflex flexion occasionally occurred.

Adductor muscle contraction occurred in the thighs of all patients with transected cords who manifested any flexor or extensor reflex activity. Contraction in these muscle groups, though quite apparent because of the prominent tendons of origin, was not unduly strong in most men. Thus, if reflex withdrawal was evoked in a supine subject, the flexing extremity rarely crossed the mid-line. Scissoring of the thighs occurred more commonly with the patient in the sitting position. When relaxation of the flexor muscles resulted in a flexed and abducted limb (*vide supra*) the sagging extremity placed stretch on the adductor tendons. In some men, clonic adductor contractions occurred and died away slowly as the weight of the extremity effected a series of lengthening reactions. Response to light percussion on the adductor tendon was always greater when the extremity was supported at the knee and the tendon slack than it was when the thighs were widely abducted and the adductors stretched maximally.

C. *Reflexogenous Zones for Flexion*

Though slight individual variation was present from patient to patient, in general there were two fairly well-defined zones of low threshold from which a flexor response could be elicited readily : the foot and the genital zone.

(1) *The foot.*—The plantar surfaces constituted a focal zone of low threshold, and a more restricted area at the toe-pad or the medial plantar surface of the arch was usually most sensitive to stimulation. Threshold was elevated slightly over the dorsal surface of the foot and in most cases there was an abrupt further increase in threshold at the ankle that was maintained over the leg and the greater part of the thigh. 19 of 22 patients exhibited maximal flexor activity when stimulated on some part of the plantar surface. All patients, without exception, demonstrated a heightened threshold for nociceptive stimulation throughout an area of the lower limb bounded proximally by the genital zone, and distally by the mid-calf.

(2) *The genital zone.*—In shape this area resembles an isosceles triangle, with the apex at the anal sphincter and the base extending between the anterior superior iliac spines. It is composed, medially, of the perineum, scrotum and penis and, laterally, of the upper, inner surfaces of the thighs and the inguinal regions. The application of nociceptive stimuli to certain cutaneous areas within this triangle evoked maximal flexor reflex activity in 3 patients, whereas similar stimulation of the plantar surface in these men evoked moderate flexion. In the remaining 19 men, though threshold for noxious stimuli was markedly less in the genital zone than on the trunk, thighs, or legs, it was considerably greater than on appropriate areas of the plantar surfaces. Within the genital zone there was evidenced a striking gradation in threshold. The region of the penile frænulum possessed the lowest threshold in practically all patients. Threshold was elevated very slightly over the glans penis and along the perineal raphe, and it was increased still more over the scrotum, the greater part of the penile shaft, and the upper, inner thigh and inguinal regions. The reactions observed as a result of the application of nociceptive stimuli to these various areas were complex, and for descriptive purposes divisible into two categories :

(*a*) *Local reaction*: Part, or all, of the following responses were observed within the genital zone as a result of nociceptive stimulation in that area. A single pin-prick of moderate intensity at the penile frænulum caused a sharp, almost instantaneous bulbocavernosus muscle contraction, evidenced by sudden retraction and relaxation at the base of the penile shaft. Though the response was usually bilateral, it was occasionally manifested only on the side stimulated. Crossed bulbocavernosus contraction as an isolated response was never observed. The bulbocavernosus reflex was succeeded almost immediately by strong, brief tightening and a slightly more delayed relaxation of the external anal sphincter. After a latent period of four to six seconds, there occurred a gradual vermicular shrinking and thickening of the integument of the scrotum. As scrotal corrugation progressed the penis exhibited simultaneous and gradual contraction to a small, tense organ. During the height of genital retraction induced in this manner, some patients complained of abdominal discomfort, or of a sensation identical to the one they experienced prior to automatic micturition. Pilomotor discharge *above* the level of cord transection occurred occasionally during the period of maximal genital response, and was closely related to the intensity and frequency of stimulation. If pin-prick had been moderately severe and, in addition, repetitive, the penile and scrotal responses were intense, pilomotor discharge more marked, and the discomfort increased. Relaxation of the scrotum and penis was then proportionately delayed, and complete flaccidity of these organs occasionally did not ensue until fifteen or twenty seconds after termination of the stimulation. An identical pattern of response was observed in the majority of patients, though thresholds varied slightly from individual to individual. Pin-prick at the

penile frænulum produced sharp, symmetrical downward contraction and equally abrupt relaxation of the abdominal recti in 5 patients. The muscle contraction was bilateral, occurred simultaneously with the bulbocavernosus response, and apparently was a specific response to nociceptive stimulation within the genital area. The frequency or the intensity of stimulation bore direct relation to the magnitude of the reflex responses obtained. Summation of less intense stimuli rarely failed to evoke responses entirely similar to those resulting from a single severe stimulus. By the proper gradation of stimulation, a bulbocavernosus reflex alone could be elicited in most patients. If intensity of pin-prick was such that contraction of the external anal sphincter was elicited, retraction of the penis and scrotum to a greater or lesser degree was usually observed.

The influence of local signature was apparent within the genital zone. Pin-prick along the perineal raphe provoked both bulbocavernosus and anal reflexes, and the strength of either response was dependent upon the skin area stimulated. The anal reflex was maximal with pin-prick of the perianal skin, whereas a maximal bulbocavernosus contraction occurred with pin-prick at the junction of scrotum and perineum. Stimulation of the skin of the upper thigh evoked all components of the local response and, as would be anticipated, application of pin-prick directly to the scrotum shortened the latency of the scrotal and penile reactions.

(*b*) *Reflex flexion*: In the majority of subjects, the application of nociceptive stimulation within the genital zone evoked withdrawal movements of the lower extremities. It is of interest that the patients invariably demonstrated responses of greater strength in the proximal musculature of the limb than in distal muscles. Movements of the feet and toes occurred rarely as a consequence of penile or perineal stimulation. Conversely, flexion of the thigh and knee was elicited fairly easily, and the movements were often executed more powerfully under these circumstances than when they were provoked by plantar stimulation. Markedly different response to slight variation of the exact locus of stimulation was noted. In some men, pin-prick along the exact mid-line of the penile frænulum or along the ventral penile raphe evoked bilateral flexor spasm, whereas a shift of the point of stimulus 2 mm. to either side of the mid-line resulted in ipsilateral withdrawal. Similar results were noted occasionally during scrotal stimulation, but here spatial discrimination was not nearly so fine, and sharp differentiation of response was frequently lacking along the perineal raphe. Crossed flexor movements were not seen. Responses were, therefore, either bilateral or were ipsilateral to the point stimulated. Two men failed to show withdrawal of the extremities or flexor muscle contraction despite the application of severe nocuous stimulation to the genital area. These subjects (P. C. and R. S.) were neurologically quite similar in that each manifested elevated thresholds for all reflex activity, and the movements elicited by various other stimuli were weak. Lack of flexor muscle response to genital stimulation was apparently

unrelated to local activity within the genital zone, however, for the reaction of the penis and scrotum in these men was identical in its intensity to that usually observed.

VII. Extensor Activity

Eighteen of 22 reflexly active patients in the group surviving cord transection for two or more years manifested predominant extensor spasms below the level of their cord lesion. A brief description of the reflex activity exhibited by each of these men below the region of cord division has been published elsewhere (Kuhn and Macht, 1949). It seems likely that movements of extensor muscles become evident as early as six months after injury, and may continue for years. Observations made on 2 men with recent cord transection and on others showing various degrees of extensor activity indicated that initial extensor contractions occurred in certain extensor muscles of the thigh and hip, and that as extension became stronger, additional muscles of the leg and thigh were activated in the reflex response. In a few men showing weak extension to maximal stimuli, contraction in the hamstrings and anterior leg musculature was invariably less marked than in the extensors of the limb, whereas in a typical patient with moderate extensor activity a maximal stimulus resulted in simultaneous contraction of all muscle groups of the lower extremity, and it was usually difficult to detect differences between the intensity of flexor and extensor muscle contraction. Patients with extreme extensor activity showed an increase in the intensity and duration of this positive supporting reaction. Under certain conditions it was possible for some of these men to stand without mechanical support. An attempt is made in the following paragraphs to further elucidate the extensor activities noted in these men, and to make some generalizations that appear to be warranted by the data at hand.

A. *The Adequate Stimuli*

The stimuli which resulted in primary extensor activity, though fairly standard from patient to patient, were considerably more complicated than those found to be most effective in the production of reflex flexion. In order of effectiveness, the following manœuvres were found to elicit primary extension of one or both lower extremities :

(1) *Extension of the thigh.*—The most provocative stimulus for the production of extensor activity in these 18 patients was a rather rapid shift from a sitting to a supine position. After a few trials, this manœuvre was carried out with agility by almost all men, and resulted consistently in sudden, smooth tightening of all skeletal musculature below the level of cord lesion. Only one subject failed to demonstrate extensor muscle responses following such stimulation. In this man, extension occurred when the patient passively hyperextended his hips, while lying supine, by thrusting up beneath the buttocks with both palms. A further demonstration of the relation of extension of the thigh to production of

extensor activity was afforded by passive lowering of the straight lower extremity while the subject lay supine. Ipsilateral or bilateral extension resulted almost invariably. A similar result was obtained in a reflexly active patient during the loose collapse of a lower extremity which had been previously stimulated to withdraw. In order to determine whether or not passive stretch of the extensors of the hip "fired" generalized extensor activity, both limbs were placed in triple flexion with the patient in a sitting position. As the subject lowered himself to his back, his lower extremities were maintained in passive flexion by the examiner, and extensor activity failed to occur. If the normal sitting position was now adopted by the patient, and passive flexion of only the thighs on the pelvis maintained as he reclined, extensor activity again failed to materialize. If one limb was allowed to remain relaxed and passively extended on the bed, and the other was held in a position of flexion at the thigh while the patient reclined, only the former exhibited extensor activity. Those men normally showing crossed extensor activity in response to tactile or proprioceptive stimulation of the lower extremities would not exhibit such activity in the passively flexed limb when subjected to the last manœuvre. Arching of the thorax, and similar contortions which place tension on the abdominal muscles, failed to elicit extensor activity. It seems certain, therefore, that the most effective proprioceptive stimulus for production of extensor muscle responses in the lower limb is stretch of the flexors of the thigh at the hip, and, in addition, that stretch of the abdominal musculature is an inadequate stimulus for such activity.

(2) *Squeezing of thigh musculature.*—In a moderate number of patients it was noted that this manœuvre, especially when the quadriceps was so stimulated, precipitated extensor activity indistinguishable in severity from that evoked by thigh extension. Mild extensor movements were thus evoked in practically all patients. The anterior thigh musculature appeared to possess a lower threshold for this type of stimulation than did the hamstring group of muscles.

(3) *Rubbing and light tactile stimuli.*—As the thresholds for stimuli effective in eliciting extensor activity decreased, reflexogenous zones widened correspondingly and, in some patients, a variety of innocuous stimuli applied to large areas of skin provoked extensor movements. Rubbing or brushing the skin of the thigh was sufficient to excite powerful primary extension in a few subjects. Mere contact with the skin overlying the popliteal space occasionally provoked ipsilateral extension which was immediately intensified by the application of slight pressure with the finger-tips. In a patient showing very low threshold and extreme reflex activity below the level of cord transection, decreased skin thresholds were found to extend distally to include the plantar surfaces, where stroking elicited primary extension and pin-prick resulted in a flexor reflex. In one or two patients, moderate extension could be induced by innocuous tactile stimulation of the perineum and scrotum.

B. *Typical Extensor Activity*

In the average patient who manifested dominant and moderately active extensor reflexes, skeletal muscle reactions to the above stimuli were fairly characteristic. As the patient lay supine with his lower extremities extended and relaxed on the bed, light contact of the fingers on the skin of the popliteal space occasionally provoked rapid, generalized tightening of the musculature in the ipsilateral extremity, locking it at the hip and knee in rigid extension. If no further movements of the hand were made, overall muscle rigidity was maintained usually for four to five seconds, and was succeeded by a slow, " plastic " relaxation progressing simultaneously in all muscle groups. Within a few seconds the rigid prop had melted to complete flaccidity. In some men it was impossible to restrict extensor activity to the ipsilateral extremity. Usually, especially when slight pressure was brought to bear at the popliteal region, bilateral extension occurred. In a patient with fairly high cord transection, this stimulus resulted in transformation of that part of the body innervated by the isolated cord into a rigid skeletal-muscular framework, the abdominal, lumbar and gluteal muscles board-like, pelvis and knees locked, lower extremities fully extended and tightly apposed, and the feet pointed. Under these conditions many discrete muscle masses were easily identifiable. Removal of stimulation resulted, after a period of approximately five seconds, in smooth and gradual subsidence of the entire rigid framework to complete flaccidity. If, on the other hand, pressure at the popliteal space was not only maintained but increased, the net result was that the full weight of the stiffened pelvis and lower extremity was borne on the supporting hand, and elevation from the bed was extremely difficult. Once the limb had been lifted into the air, with support limited to a minimal point in the popliteal region, the effect of gravity resulted in an eventual slow, passive flexion of the leg at the knee and of the thigh at the pelvis. Though this process was usually a smooth and gradual one, occasionally the limb subsided jerkily, executing a series of hopping movements, each of which resulted in a slight increase of flexion. When flexion of the thigh and leg had reached approximately a right angle at the pelvis and knee, respectively, complete flaccidity of the extremity ensued, with the notable exception of the adductor musculature. The leg was then freely mobile at the knee, and the thigh could be rotated through all positions except abduction without exciting reflex activity. If, in this position of flexion, the feet were placed passively in apposition on the bed, and support removed from the extremities, complete spread-eagling would eventually follow either gradual relaxation of the adductors, or a series of lengthening and shortening reactions involving those muscles.

Extensor responses in the contralateral limb were common. Dependent upon the vigour of extensor activity and the threshold of the patient, crossed extension occurred in some instances so rapidly that it appeared to be synchronous with ipsilateral extension, and in others only after a latent period of as much as two to three seconds. In a few of the men

with quite severe extensor activity, light touch on one plantar surface was sufficient to immediately convert the entire musculature below the cord lesion into a rigid framework. In the few patients showing weak flexor and extensor activity, typical primary extension of the ipsilateral limb occurred frequently with no involvement of the abdominal musculature. It was interesting that these particular subjects would exhibit occasional moderate crossed extensor activity after having been bedridden for a short time, or during the onset or course of a transient illness. In addition, postural stimulation (the assumption of the erect position) in those patients ordinarily displaying minimal reflex activity in their skeletal musculature would frequently evoke a more or less sustained tightening of the lumbar muscles, pelvis, and both lower extremities. Though vigour of the response was much less than in other men, the characteristic rapid tightening, prolonged contraction, and smooth, gradual relaxation of the musculature was maintained.

A number of reflex activities were elicited by special manœuvres. The lengthening and shortening reactions in the quadriceps muscles were demonstrable in almost all men, and the clasp-knife phenomenon occurred commonly at termination of forced passive flexion of the lower limbs. With the thighs flexed passively to 90 degrees at the pelvis, and the lower extremity flaccid in the "clasp-knife" position, forceful apposition of the leg to the posterior surface of the ipsilateral thigh resulted usually in palpable increase of tonus in the extensor muscles of the contralateral limb (Philippson's reflex). Occasionally this manœuvre provoked severe primary extension of the contralateral limb, maintained for as long a period as pressure was exerted. Forceful passive extension of the leg when the thigh was supported at a right angle to the pelvis resulted in an initial, enduring contraction of the hamstrings in the contralateral limb. With further elevation of the leg, sharp, jerking flexor spasms occurred, and an abrupt flexor withdrawal might result. Cessation of pressure yielded an immediate crossed decrease in hamstring tonus.

In several of the men exhibiting marked extensor activity, slight but broad pressure against the toe-pads of an extremity partially flexed at the hip and knee resulted in immediate powerful, driving thrust, and simultaneous sharp loss of tone in the contralateral extensors. Release of plantar pressure was followed by flaccidity of the limb if it had not been permitted to stiffen too far toward full extension, for it was found that if the extremity were allowed to reach within 30 to 40 degrees of complete extension, extensor thrust was augmented by contraction of the combined muscles of the pelvis and thighs, and primary bilateral extension would then result. In only one patient was it possible to elicit classical "stepping" movements, and these appeared, at certain times, to be self-propagated.

VIII. Representative Protocols

During the period of observation, 2 men exhibited flexor spasms

alone; 2 showed approximately equal flexor and extensor spasms; and 18 displayed predominant extensor spasms. The following case reports were selected to show the typical neurological findings in subjects from each of these groups, and, in addition, to illustrate the minor differences in reflex flexion activity which may be present from patient to patient.

The neurological findings in the following patient are representative of those usually observed in a subject with predominant extensor reflex activity.

Case 3.—*The typical reflex pattern noted in* 18 *men. Predominant extensor and moderate flexor reflex activity two years after cord transection.*

P. P., aged 21, received multiple machine-gun wounds on February 1, 1945, and was immediately and completely paralysed below the level of the nipples. X-rays disclosed a comminuted fracture of the fifth dorsal vertebra. Exploratory laminectomy on February 2, 1945, revealed a compressed but intact cord at that vertebral level. On January 29, 1947, prior to an anterior rhizotomy, re-exploration showed a large syringomyelitic cavity in the cord at D–5. The sac was excised, leaving two slightly scarred stumps with a 2 cm. gap between them. There was no indication that this procedure altered the neurologic picture in any way. The cutaneous level of anæsthesia remained at the upper edge of the D–5 dermatome bilaterally.

The following examination was conducted two years after injury, and one month after excision of the syringomyelitic sac.

Physical appearance.—The patient is examined in the supine position. Rectal temperature is normal. An inlying urethral catheter is in place. Body build is medium. The trunk and lower extremities appear normal in size and configuration. The muscle masses of the hips are slightly wasted. There are no décubiti and the skin is cool and dry. Spontaneous involuntary movements are not noted. The lower extremities lie relaxed, fully extended, and rotated slightly outward at the hips, with the feet in a position of limp plantar flexion. There is no œdema. There is a one-inch band of hypæsthesia at the upper margin of the D–5 dermatome anteriorly and posteriorly. Below that level loss of cutaneous and other sensibility is complete.

Reflex flexor activity.—Threshold is quite low over the plantar surfaces. Plantar stroke or pin-prick results in abrupt, jerking responses which occur after a very brief latent period. These movements increase in range and strength with increase of the intensity or frequency of stimulation. The following activity is evoked by means of a single stimulus of moderate strength: Initial strong dorsiflexion of the ipsilateral hallux, and less marked dorsiflexion of the remaining four toes, succeeded almost immediately by abrupt dorsiflexion of the foot. There is sharp contraction of the sartorius and tensor fasciæ latæ muscles, noticeable especially a short distance below the anterior superior iliac spine. Simultaneously, the medial hamstrings and the ipsilateral lumbar and posterior abdominal muscles tighten, and the contralateral lower limb stiffens into extension with the foot in strong plantar flexion. During maximal response, therefore, the rib cage twists down abruptly toward the side stimulated. Movements are extremely abrupt, but the phase of flexor muscle relaxation appears to be more rapid than that of contraction. A mild plantar stimulus elicits only fragments of the complete response, i.e. ipsilateral hallux and toe movements alone occur, or, with slightly stronger stimulation, dorsiflexion of the foot may be added. Muscle contractions in the ipsilateral thigh and lumbar areas, and in the contralateral lower extremity appear to be simultaneous. Severe plantar stimulus produces a quick, hopping withdrawal of the ipsilateral lower limb, combined with a sharp, downward movement of the rib cage on that side,

and generalized extensor stiffening of the musculature in the contralateral limb. The reflexogenous zone for flexion is maximal at the plantar toe-pad ; is increased slightly over the remainder of the sole ; and elevated still more over the dorsum of the foot. The application of strong nocuous stimulation to the legs or thighs rarely elicits movements of any type. The ventral abdominal musculature remains completely flaccid unless extensor responses supervene.

Direct nociceptive stimulation of the abdominal wall evokes no response. Abduction of the thighs with the legs in the flexed position evokes reflex adductor tightening, and lengthening and shortening reactions of the adductor musculature can be demonstrated.

Mild pin-prick of the glans penis elicits a vigorous bilateral bulbocavernosus reflex. Stronger stimulation to the surface of the glans evokes a sharp bulbocavernosus reflex, strong tightening of the external anal sphincter, and an abrupt, jerking flexion of the ipsilateral lower extremity. After a brief interval, there is slow, generalised shrinking of the scrotum and penile shaft. The only responses to maximal stimulation of the penile frænulum at the mid-line are delayed scrotal corrugation and slow retraction of the penile shaft. Pin-prick at the upper, inner surface of the thigh evokes local genital activity and, in addition, an ipsilateral flexion response, more readily than does a similar stimulus within the genital zone. Shrinkage of the penis and scrotum is more rapid and marked as a result of thigh stimulation. The reflex flexion elicited is quite different from that evoked by plantar stimulation. Movements of the feet and toes do not occur, and crossed extensor activity is absent. Contraction of the same flexor muscles in the thighs and lumbar areas is stronger and more prolonged. Pin-prick of moderate intensity at the pubic area induces scrotal and penile shrinkage alone. Accompanying all nocuous stimuli of moderate intensity to the genital and anal areas is a sensation of " impending spasms " and what the patient terms " a forerunner of headache." There is no apparent pilomotor activity. The sensations experienced show a latency of 6–10 seconds, and persist for approximately the same length of time after stimulation is terminated.

Reflex extensor activity.—This type of reflex activity is the predominant pattern manifested below the level of cord division. Responses are elicited most easily by moving the patient from a sitting to a reclining position. There is immediate, generalized extension and sustained muscle rigidity from the level of the xiphoid distally. The feet are plantar-flexed and the thighs tightly adducted. Plastic relaxation proceeds simultaneously in all muscle groups after a period of 5–8 seconds. Ipsilateral extension involving the trunk and lower limb is elicited by allowing the flexed, flaccid limb to slide of its own weight to a position of extension. Similar but more fleeting extensor activity is provoked by squeezing the musculature of the thigh. Crossed extensor movements with the latter manœuvre are rare.

Comment.—This man is presented as a typical representative of the large group of patients in stage 5, i.e. those who exhibited predominant extensor activity below the level of cord lesion two years or more after injury. The description of the reflex flexor activity in this patient will apply, in general, to almost any member of that entire group. As was true with many other subjects, he displayed a number of activities which were unusual for the group as a whole. For example, contralateral extension evoked by plantar stimulation ; dorsiflexion of all toes with pin-prick to the sole ; and the very low threshold area at the upper, inner thigh, were not usual findings. In general, however, the thresholds for reflex flexion and the vigour and form of flexor movements in this patient were identical with those observed in the majority of men sustaining cord transection of long duration.

Within the group of 18 men showing typical reflex activity, though extension was always the dominant pattern, the strength and complexity

of reflex responses varied. The extreme limits of variation in responses are well exemplified by the patterns elicited in the following two cases :

Case 4.—*Reflex extensor activity and minimal flexion movements two and a half years after cord transection.*

R. S., aged 22, was injured by a bullet on January 8, 1945. He sustained an immediate paralysis below the level of the nipples. X-rays revealed a fracture of the body and laminæ of the second dorsal vertebra. Laminectomy on the day after injury disclosed a completely pulped and liquefied cord at the lower border of the second dorsal vertebra. The liquefied matter was removed, leaving a gap of several cm. between the rostral and caudal cord ends. The sensory level on the day following surgery was stated to be sharply demarcated at the lower border of the D–2 dermatome.

The following examination was conducted two years and eight months after injury.

Physical appearance.—The patient is examined lying supine. He is afebrile, free of a urethral catheter, and there are no decubitus ulcers. Body build is medium, and the trunk, hips, and lower extremities appear normal in size and configuration. The skin is cool, and a normal flare follows local pressure. The lower limbs are extended limply on the bed with the feet moderately plantar-flexed, and each extremity is rotated slightly externally at the hip. There is a suggestion of fullness in the tissues covering the dorsum of each foot, and tendon markings of the extensor digitorum longus are indistinct, but there is no œdema. There is no spontaneous involuntary activity. A band of hypæsthesia occupies the D–2 dermatome anteriorly and posteriorly, and there is complete cutaneous anæsthesia below that level.

Reflex flexor activity.—It is possible to elicit a weak, incomplete flexion reflex by stimulation of the plantar surface. Pin-stroke appears to be a more effective stimulus than pin-prick. Visible muscle movements are restricted to the toes, feet, and calves, though slight contraction is palpable in the appropriate muscle masses of the thigh. Plantar stroke or pin-prick of moderate severity results in immediate marked fanning and flexion of the ipsilateral four toes, accompanied by mild dorsiflexion of the hallux. The foot dorsiflexes moderately, and tightening of the medial hamstring muscles occurs. Simultaneously the tensor fasciæ latæ and sartorius muscles ridge up slightly just below the anterior superior iliac spine. There is no movement of the knee-joint, and the contralateral limb remains completely flaccid. At no time is there activity in the abdominal or paravertebral musculature. Movements resemble muscle twitches, and contraction and relaxation is quite abrupt, with no evidence of after-discharge. The limbs are limp and all joints freely mobile. There is moderate adductor tautness, but with the legs flexed the thighs can be slowly parted to expose the perineum. With gentle abduction the adductor longus tendons slowly rise to form a prominent ridge at the lower border of the pubis. Rubbing the skin overlying either tendon occasionally provokes sudden bilateral adductor contraction, swinging the thighs into apposition. The most powerful stimulus is a sharp tap with a percussion hammer. Immediate adduction occurs, with evidence of considerable after-discharge. If the weight of the flexed and slightly abducted limbs is allowed to carry them laterally, a series of slow lengthening and rapid shortening reactions occur, resulting eventually in complete quiescence of the extremities in a position of extreme abduction. There is then no response to percussion of the adductor tendons. Adductor muscle activity is not accompanied by other involuntary muscle contraction.

Pin-prick stimulation of the flaccid penis evokes strong, bilateral bulbocavernosus reflexes, wrinkling-in of the external anal sphincter, and penile and scrotal shrinkage. If the stimulus is applied to the penile frænulum, penile retraction occurs within 3–4 seconds, and scrotal corrugation follows shortly. Perineal or scrotal pin-prick

results in activity of the scrotal dartos almost immediately, but penile shrinkage does not begin for 6–9 seconds. Involuntary movements of the trunk and lower limbs are completely absent, despite severe stimulation of the perineum, or of the penile glans or frænulum.

The presence of penile erection is accompanied in this patient by a sensation of a " cold wave " across the upper pectoral region, and pin-prick to the organ results in sudden intensification of the sensation. Pilomotor erection and multiple pectoral muscle fasciculations occur throughout a broad band below the clavicles. Except for differences in intensity of discomfort, the patient is utterly unable to differentiate between the sensation produced by erection, and that resulting from pin-prick of the frænulum or glans of the penis, or from digital stretch of the anal sphincter.

Reflex extensor activity.—Extensor movements below the level of cord transection, though attenuated, were stronger than flexion responses. Primary extension could be precipitated by lowering the patient from a sitting to a supine position, and was manifested by rapid tightening of the musculature of the trunk, pelvis, and lower extremities. Rigidity was not well maintained, however, and relaxation occurred within a few seconds. Rapid lowering of the elevated extremity to the bed resulted in generalized quivering extension of the ipsilateral limb, but crossing was rare and quite incomplete when it did occur. Rubbing or squeezing the skin of the thighs elicited no responses.

Comment.—This patient and one other in the group with chronically transected cords are of interest in that they exhibited what was termed " minimal flexion movements." Gross movements of the lower extremities at the joints did not occur despite the application of maximal nocuous stimulation to receptive fields for reflex flexion. It was notable that, though the threshold for nocuous stimuli was quite high over the soles, threshold was so elevated in the genital zone that no movements whatsoever occurred. In no other patient exhibiting reflex activity below their cord lesion was this lack of response to noxious stimulation in the genital zone observed. Local genital response, however, was elicited easily, and did not show apparent increase of threshold. Genital reflexes seemed to be quite marked in this man. Extensor muscle activity was rated as 2^+, but these responses also displayed a moderately heightened threshold to various stimuli. Though manifestations of skeletal muscle activity in the limbs and trunk were thus selectively attenuated, there was a striking absence of atrophic changes in the musculature innervated by the isolated cord.

Case 5.—*Extreme extensor responses and moderate flexor activity three years after cord transection.*

T. McC., aged 32, was struck in the chest by a shell fragment on October 30, 1944. There was immediate, complete loss of all sensations and motor power below the level of the nipples. X-rays revealed comminuted fractures of the laminæ of D–5 and D–6, with fractures of the vertebral ends of the right fifth and sixth ribs. Exploratory laminectomy on February 14, 1947, disclosed a complete absence of spinal cord substance at the vertebral levels of D–3, D–4, and D–5.

The following examination was conducted two years and five months after transection of the cord.

Physical appearance.—This muscular young male is in excellent physical condition. He is examined lying supine. There are no decubiti, rectal temperature is normal, and the patient is catheter-free. Body build is stocky, and there is remarkably little evidence of wasting below the level of cord transection. The skin is warm and dry over the entire body. The skeletal musculature below the level of cord transection is in an extremely active state.

Reflex skeletal muscle activity.—Flexor responses, though similar to those observed in other subjects, were invariably modified in this patient by complex extensor

activity. Flexor activity is described below, therefore, only in its relation to the extensor movements evoked by various stimuli.

The act of reclining supine on a flat bed initiates a complex series of muscle movements below the level of cord injury. The lower extremities, observed throughout a period of ten minutes, maintained continual motion. The involuntary activity manifested by this man is unlike the stereotyped flexor and extensor activity seen in most other subjects. Strong, smooth, and relatively slow muscle contractions draw one limb up into moderate flexion at the knee and pelvis. The extremity remains suspended, oscillating slowly from one side to the other at the hip, while the contralateral limb gradually stiffens out into rigid extension. The pattern then changes, the flexed extremity slowly drops lower until the heel contacts the bed. There is an immediate reaction. The contralateral limb draws smoothly up into flexion while the stimulated limb straightens out into extension, or both lower extremities may jerk powerfully into the air and begin to wave slowly about at the hips with the knees partially flexed. Frequently both limbs stiffen into extension, and the powerful, squeezing muscular contraction involving the belly and torso elicits a sudden expiratory grunt from the patient. Flexion phases are characterized generally by abduction and occasionally by marked spread-eagling of the thighs, the extensor phases by strong adduction. Attempts to handle the extremities during this period of activity are met by bursts of powerful, alternating flexion and extension, and the limbs become momentarily completely unmanageable. Contact of the feet with the bed appears to evoke less and less reaction, and the extremities eventually subside until they lie flaccid in the fully extended position.

The threshold distribution for stimuli productive of the " pillar-like " rigidity exhibited by this patient may be outlined as follows: Light stroke seems to be the most effective stimulus. The highest thresholds lie over the upper abdomen, dorsum of the feet, and lateral surface of the legs. The medial surface of the leg is fairly sensitive and the lower, inner thigh moderately so. However, the plantar areas, anterior and lateral thigh surfaces, and hypogastrium are equally responsive. The upper, inner thigh, perineum, and posterior lower thigh and popliteal regions exhibit the lowest thresholds. The buttocks, lumbar areas, and calves are relatively insensitive.

Immediate response to light brush along one plantar surface is a generalized lower extremity extensor rigidity which becomes bilateral a split second following stimulation, and involves the entire abdominal and lumbar musculature. If intensity of the stroke is increased, bilateral rigidity is followed by rapid abduction of the ipsilateral extremity which lifts slightly from its taut hinge at the pelvis and swings outward. In most instances there is a latent period of perhaps one second before the contralateral limb lifts and swings in the same direction, maintaining close approximation to its fellow. If the elevated limbs swing fairly far (30–40 degrees) to right or left of the longitudinal axis of the body, they slowly return and overshoot the mid-line, moving from side to side through shortening arcs like a slowing pendulum. Eventually the extremities hover momentarily at the exact mid-line, then lower to the bed and rigidity gradually melts. Frequently, if one sole is stimulated, that extremity will flex strongly at the foot, knee and hip, and as it relaxes will slide down to enter into (1) another phase of triple-flexion with the thigh widely abducted, or (2) extensor rigidity which almost immediately becomes bilateral and the stiffened limbs then lift slightly and oscillate from one side to the other in the manner described, or finally, (3) complete extension of the relaxing limb and simultaneous contralateral triple-flexion.

It is impossible to lift either extremity at the popliteal space without exciting rigidity, for generalized extension occurs with mere contact of the fingers in that region. If, despite the resistance, the stiffened extremity is lifted into the air, relaxation eventually occurs, and the limb will remain limp so long as the heel is prevented from contacting the bed. One or two fingers can now be placed on the

toe-pad area and the touch evokes no reaction. When gentle pressure is brought to bear on the pad, however, the quadriceps tightens instantly, the thigh extensors contract, and a strong extensor thrust slowly drives the resisting hand before it. Simultaneously there is overall lessening in tone in the muscles of the contralateral extremity. Removal of plantar pressure during the early phase of this activity results in relaxation in the flexed position, and the opposite limb resumes its original spasticity. If the thrust straightens the limb out within about 30 degrees of complete extension, extensor rigidity will ensue despite removal of the stimulus, and is invariably bilateral. Light stroke of the scrotum or perineum produces moderate generalized extension involving all muscle groups. The threshold becomes much higher posterior to the anal sphincter and above the neck of the scrotum. Reaction to light stroke at the perianal region, or the area immediately surrounding the base of the penis is slight. Though handling of the scrotum elicits immediate extensor activity, such activity will not follow handling of the penis unless surrounding areas are inadvertently contacted.

Pin-stroke at the upper, inner thigh elicits a series of complex activities. With increasing strength of stimulus there is an initial strong cremaster contraction, lifting the testicle high in the scrotum ; generalized extensor rigidity and abduction of the ipsilateral limb ; contralateral cremaster response, less strong than that on the ipsilateral side, together with crossed extensor rigidity ; and synchronous abduction of the stimulated limb and adduction of the contralateral limb, swinging the rigid lower extremities toward the side stimulated. Tactile or pressure stimuli applied to the thighs yield essentially the same responses but with increased thresholds.

Direct nociceptive stimulation of the glans penis is the most effective procedure for evoking cremaster, bulbocavernosus, and anal sphincter reflexes. When the mid-line is pricked, there is sharp, symmetrical testicular retraction ; an abrupt contraction and relaxation of the bulbocavernosus muscles together with a short, jerking penile retraction ; and a strong anal reflex. By modifying the strength of stimulation a bulbocavernosus contraction can occasionally be produced alone. Strong pin-prick elicits a typical triple-flexion of both lower extremities, and the usual delayed retraction of the scrotum and penile shaft. During retractile activity the patient complains of a sudden sensation of being on the verge of urination.

Testicular retraction is an excellent and reliable indicator of extensor activity in this patient. Strong contraction of the cremaster muscles always accompanies generalized extension, and the degree of bodily rigidity seems a reflection of hyperactive cremaster reflexes which are thrown into action whenever skeletal muscle response occurs. It is an entirely different phenomenon than the slow retraction characteristic of delayed genital responses.

Comment.—This patient illustrates the truly remarkable skeletal muscle activity that may be manifested following a high thoracic transection of the cord. The stepping and " bicycling " movements he occasionally exhibited were described by other patients as occurring in their extremities also, but during an earlier period, prior to the time they came under observation.

The following protocols are presented to show some unusual deviations from the typical reflex patterns that develop after transection of the cord.

Case 6.—*Absence of extensor activity in a patient with cord transection of long duration.*

R. B., aged 28, was struck in the chest and spine by a bullet on October 7, 1944. There was immediate sensory and motor paralysis below the level of the nipples. No bony fractures occurred. An exploratory laminectomy on September 25, 1945, revealed a crushed cord at the level of the D–5 vertebra. The dura and scarred proximal and distal ends of the cord were completely excised, leaving a considerable gap in the spinal canal. Judging from pre- and post-operative examinations, this extirpation did not alter the neurologic status of the patient in any way. The level

of cutaneous anæsthesia remained at its original level below the D–4 dermatome on the right, and D–5 on the left.

The following examination was conducted three years after cord transection.

Physical appearance.—The patient is examined lying supine. Rectal temperature is normal and there is an indwelling urethral catheter. Severe, generalized atrophy of the muscles of the trunk and limbs below the level of cord lesion is apparent. Mild flexion contractures at the hips, and chronic flexion contractures at the knees of approximately 25 degrees are present. The limbs are, consequently, in a position of permanent flexion, and fall to one or the other side when the patient reclines. Massive scarred areas covering the femoral trochanters show a hyperemic surface epithelium of tissue-paper thinness. The sacral area has much the same appearance but is covered with a layer of pink, clean granulation. The extensor musculature of the thighs is represented by a few thin fibrous bands palpable beneath the skin. The medial hamstring tendons stand out prominently along the distal aspect of each thigh. There is a band of hypæsthesia at the level of D–4 on the right and D–5 on the left, and complete cutaneous sensory loss below those levels.

Reflex flexor activity.—The lower extremities differ considerably in threshold for nocuous stimulation. On the right, the ball of the foot constitutes the area of greatest sensitivity, while the dorsum of the foot, the entire leg, and much of the surface of the thigh has a much higher threshold. Movements of the hallux do not occur when the plantar surface is pricked, but there is moderate dorsiflexion of the remaining four toes, strong dorsiflexion of the foot, and tugging contraction of the tensor fasciæ latæ, iliopsoas, semimembranosus, and gracilis. No crossed responses were obtained. The upper inner thigh has a lower threshold than the thigh surfaces immediately below or laterally, and triple-flexion movements are elicited fairly readily by stimulation at this point. On the left, though lowest thresholds are present along the plantar surface, stroke or pin-prick elicits no movements of the foot or toes. In other respects the activity elicited is an attenuated replica of that evoked in the contralateral extremity. In addition, the left adductor longus tendon appears to tighten slightly as withdrawal is initiated. None of these flexor movements are of sufficient strength to jerk the thigh beyond a right angle at the pelvis. Tactile and nocuous stimulation of the skin of the buttocks, lumbar region and abdomen fails to provoke muscle activity. Extensor activity is lacking completely.

Pin-prick of the glans, frænulum, or shaft of the penis elicits a sudden bulbocavernosus reflex, contraction of the anal sphincter, and sharp, jerking movements of triple-flexion. With mid-line stimulation, both lower extremities respond. Deviation 5 mm. to either side of the penile or perineal raphe evokes ipsilateral withdrawal. The usual delayed scrotal corrugation and penile retraction follow nocuous stimulation in the genital zone, and the effects persist a considerable period after cessation of the stimuli. Rubbing the scrotal integument induces occasional bilateral medial hamstring contraction.

Comment.—In this patient, flexor activity alone was elicitable below the level of cord lesion. One other man was unusual in that he, too, had progressed only to the stage of flexor activity since his lesion was incurred. Both subjects exhibited severe fibrous atrophy of the extensor musculature of the thighs and legs and, in each, flexion contractures at the hips and knees were slowly progressive. Originally violent flexor activity became limited by ankylosis. Thus, in time, many other patients who manifested varying degrees of extensor activity exhibited, in addition, far more range and strength in flexion responses than did either of these men.

Atrophy at the hips was marked in these two patients. The overall clinical picture was one of selective atrophy in the skeletal musculature below the level of cord lesion, progressively severe flexion contractures involving the large joints of the lower extremities, and chronic or recurrent decubitus ulcers. The degree of permanent joint deformity appeared to depend upon the stage at which measures were taken to eliminate flexor muscle activity.

Case 7.—Equal reflex flexor and extensor activity manifested three years after cord transection.

W. M., aged 23, was injured July 13, 1944, by a rifle bullet which severely traumatized his left upper arm, and eventually lodged within the spinal canal at the level of the tenth dorsal vertebra. It was necessary to amputate the left upper extremity about 6 inches below the axilla. Laminectomy at the site of injury three days later disclosed a " contused " cord. Re-exploration on February 12, 1947, revealed a dense scar within the spinal canal at the level of the tenth dorsal vertebra. This scar was excised, leaving a 2 cm. gap between the proximal and distal stumps. Pre- and post-operative neurologic examinations revealed no significant changes in the status of the patient. His cutaneous sensory level was sharply demarcated at the lower border of the D–10 dermatome, with complete anæsthesia below that level.

The following examination was carried out three years after injury.

Physical appearance.—The patient is examined lying supine. There are no decubitus ulcers, rectal temperature is normal, and an inlying urethral catheter is present. Body build is slight. The legs and thighs are cold and wet with sweat. Normal reclining position is with the right limb almost completely extended, whereas the left is maintained in moderate flexion and crossed slightly over the knee of its fellow. Spontaneous involuntary movements do not occur. The D–10 dermatome is occupied by a band of hyperæsthesia, and anteriorly and posteriorly there is complete cutaneous anæsthesia below that level.

Reflex flexor and extensor activity.—The left lower extremity rests in a position of partial flexion at the knee and hip. Thigh flexors are under moderate tension. The left hallux is chronically dorsiflexed. Slight stimulation in the form of light contact with any part of the foot, and especially with the sole, results in further violent dorsiflexion of the hallux, accompanied by fanning of the toes with tremulous side-to-side movements. As strength of stimulation increases there is a sharp, jerking flexion of the leg on the thigh, and the latter on the pelvis, but a position of acute triple-flexion is not maintained. Relaxation is abrupt, and the limb flops loosely to its characteristic resting position, though all muscles do not become equally flaccid, i.e. the adductors of the thigh maintain a strong, sustained tension. If the forepart of the foot is grasped and the lower extremity lifted into the air, violent ankle and quadriceps clonus results. These movements eventually subside spontaneously. As slight, persistent pressure is applied against the toe-pad area there is a generalized increase in extensor tonus, and an extensor thrust develops and gradually increases in strength. Within a few moments the limb stiffens out into complete rigid extension, with the foot strongly plantar-flexed. If pressure being applied to the sole is released suddenly, there occurs prompt lessening of quadriceps tension, the limb becomes mobile, and tends to flex at the knee and hip. With more gradual release of plantar pressure the limb rigidity melts more slowly. The thigh adductor musculature is not found to relax with any manœuvre. Exertion of tension on these muscles by drawing the thighs apart forcibly results, consistently, in rebound adductor spasm.

The right lower extremity exhibits predominant extensor activity. Stroking of the plantar surface will elicit response only when the stimulation is severe, and then contraction of the ipsilateral thigh adductors occurs, followed almost immediately by crossed adductor spasm. Manipulation of the hallux or toes elicits no activity, in marked contrast to the powerful flexion movements evoked by a similar manœuvre on the left. Pin-prick of the plantar surface evokes quivering twitches of the hallux and occasionally a short, sharp dorsiflexion of that digit. Slight fanning and tremulous movements occur in the remaining toes during such stimulation. Severe pin-prick of the right planta evokes abrupt, jerking, triple-flexion which possesses neither the range nor force of the response noted in the opposite extremity. It is during relaxation from this induced, incomplete triple-flexion that the right lower

extremity develops pillar-like rigidity not seen in its fellow except during special manœuvring.

Hyperflexion of the left leg on the thigh elicits generalized extension in the crossed extremity much more easily than it is produced by similar flexion of the right leg. Thus, threshold is found to be greatly decreased for nocuous cutaneous stimulation throughout the left lower extremity, and increased on the right, whereas the thresholds for elicitation of extensor movements are the reverse. Despite the increase in threshold for nociceptive stimuli on the right, the same relative differences in thresholds in different areas are noted in that limb, i.e. the plantar surface, and especially the skin at the medial side of the toe-pad, demonstrates lowest threshold for flexor responses.

Pin-prick of the penile frænulum elicits a brisk bulbocavernosus reflex ; slightly delayed but vigorous contraction of the external anal sphincter ; a sharp downward contraction of the abdominal recti ; and the usual latent interval prior to scrotal and penile retraction. A bilateral triple-flexion reflex occurs with strong stimulation. Ipsilateral abdominal rectus response is evoked readily by pin-prick of one or the other side of the glans penis. Reflex flexion results frequently from such stimulation, the response being either unilateral or bilateral dependent upon whether the stimulus is mid-line or to one side. Strong bilateral abdominal contraction is elicited best by mid-line scrotal pin-prick.

Comment.—This patient presented a remarkable combination of reflex activities. He was the only individual in the chronic group with cord transection to display a marked preponderance of extensor activity in one lower extremity and an equally vigorous and dominant flexor pattern in the opposite limb. It is notable that, though flexor muscle hypertonicity maintained the left limb in continual, partial flexion, full extension of that limb could be provoked by manipulation, and the extensor thrust which was developed was of surprising strength. Atrophy of skeletal muscles below the level of cord transection in this man, and in one other with similar reflex manifestations, was slight. There was no difficulty, however, in perceiving a difference in limb size from those patients who displayed predominant extensor movements. The slight atrophy noted, though generalized, was in no way comparable to the severe emaciation characteristic of the completely flaccid subjects.

IX. Penile Erection and Ejaculation

There was a sharply circumscribed reflexogenous area for the elicitation of penile erection which included the corona of the glans and the penile frænulum. Gentle rubbing of the skin or slight movements of the prepuce over this small area proved to be the most effective stimulus, and almost invariably evoked complete penile erection within 30 seconds. Rubbing or manipulative stimulation was rarely effective when restricted to the remainder of the shaft of the penis, and in no patient was erection produced directly by the application of varied tactile and proprioceptive stimuli to other areas of the genital zone, trunk, or lower extremities. Once elicited, it was possible to prolong erection indefinitely by continuous, non-nociceptive stimulation at the low-threshold loci described. One subject (P. C.) stated that, in his case, erection was facilitated by massage of the penile shaft at its base, and examination corroborated this claim. It was found that the receptive field for erection in this subject was considerably less limited than it was in the other men, for although complete erection could be induced by stimulation at the frænulum, it occurred much more rapidly following manipulation at the base of

the penile shaft. Other patients claimed to have an increase in the number of erections while they carried an inlying urethral catheter. During examinations, the presence of a catheter within the urethra was not productive of an erection, nor did one occur if the catheter was moved gently back and forth within the canal. Rubbing the edges of the meatus usually elicited turgor, however, and gentle friction at the low-threshold field caused rapid swelling of the organ.

Erections could be induced invariably if there was evidence of reflex activity below the level of cord lesion (Table IV). 4 of the chronically flaccid men referred to in an earlier part of this report had not noted penile erections since the day their lesion was incurred, and various stimuli applied during examinations failed to elicit any evidence of penile activity. 22 of the 25 patients manifesting reflex activity in the region innervated by their isolated cord demonstrated complete penile erection when the proper stimulus was applied. The remaining 3 men developed incomplete erections during examinations, but stated that erections were, at other times, quite complete.

TABLE IV.—GENITAL REFLEXES IN 25 MEN WITH VERIFIED ANATOMIC TRANSECTION OF THE SPINAL CORD

Pt.	*Level of cord lesion*	*Penile erections*	*Bulbo-cavernosus reflex*	*Cremasteric reflex*	*Subjective sensations (assoc. with erection)*	*Ejaculation*
1	D–2	Complete	Strong	Absent	" Cold wave "	Occasional
2	D–2	Incomplete	Weak	Absent	Absent	Not noted
3	D–3	Complete	Moderate	Moderate	Absent	Not noted
4	D–3	Complete	Strong	Strong	" Aching "	Not noted
5	D–3	Incomplete	Moderate	Absent	Absent	Not noted
6	D–4	Complete	Strong	Strong	Absent	Not noted
7	D–4	Complete	Moderate	Absent	Absent	Induced once
8	D–5	Complete	Moderate	Absent	Absent	Not noted
9	D–5	Complete	Moderate	Absent	Absent	Not noted
10	D–5	Complete	Strong	Strong	Absent	Not noted
11	D–5	Complete	Strong	Absent	" Burning "	Not noted
12	D–5	Complete	Moderate	Absent	Absent	Not noted
13	D–6	Complete	Strong	Strong	Absent	Not noted
14	D–6	Complete	Weak	Absent	" Burning (?) "	Not noted
15	D–7	Complete	Moderate	Absent	Absent	Not noted
16	D–8	Complete	Strong	Absent	Absent	Not noted
17	D–8	Complete	Strong	Strong	Absent	Not noted
18	D–8	Complete	Weak	Absent	Absent	Not noted
19	D–9	Complete	Moderate	Absent	Absent	Not noted
20	D–9	Incomplete	Weak	Weak	Absent	Not noted
21	D–9	Complete	Strong	Absent	Absent	Not noted
22	D–10	Complete	Moderate	Absent	" Fullness "	Not noted
23	D–10	Complete	Moderate	Absent	Absent	Not noted
24	D–10	Complete	Strong	Absent	Absent	Not noted
25	D–12	Complete	Moderate	Absent	Absent	Not noted

Priapism unrelated to cutaneous stimulation was not seen in these chronic spinal men, though it was present for a brief period immediately

after injury in one of the two patients with recent cord transection. It is doubtful if the penile erections observed in any of these subjects were ascribable to other than cutaneous stimuli. When the patient with persistent penile erection was stripped and all extraneous contact, such as bedclothes or a urethral catheter, removed from the penis, erections subsided promptly. Moreover, during the course of many different examinations, no patient failed to show slow but progressive detumescence of the penis beginning immediately after cessation of stimulation; in short, penile erections never occurred in the absence of a specific stimulus.

In general there was a fairly close correlation between the vigour and frequency of skeletal muscle activity and the frequency of penile erection in these men. Thus, most men first became aware of an increase in the duration and number of erections as flexor spasms intensified, and of even more frequent and sustained penile activity when extensor movements supervened. That this correlation between generalized skeletal muscle activity below the cord lesion and penile erections was not invariable was indicated by the frequent and undiminished penile erections evidenced by two subjects (R. S. and P. C.) who displayed quite weak and attenuated skeletal muscle activity. Apparently the activity of the isolated cord as manifested by the frequency and intensity of skeletal muscle movements is not always an indication of the frequency and intensity of reflex penile erection. A proof of the lack of relation of skeletal muscle activity *per se* to penile erections was afforded by selected patients who had undergone anterior dorsolumbar rhizotomy. A few of these men reported a definite *increase* in the frequency and duration of erections, despite the post-operative findings of complete flaccid paralysis of the lower extremities and greatly decreased abdominal and lumbar muscle spasm.

None of the patients with cord transection experienced a specific sensation by which they were able to recognize a penile erection. Special precautions were taken during examinations to exclude visual and other sensory clues. 21 men experienced no sensation whatsoever in association with erection. 4 subjects, who had chronically survived cord transection, reported vague sensations (Table V). J. Z. experienced a numb, aching "tightening" deep in the abdomen just above the pubis during full erection, but proved unable to differentiate a similar sensation induced by stretch of the internal anal sphincter. He differentiated quite consistently a perineal "burning sensation" evoked by nocuous stimulation in the genital zone. R. S. experienced a "cold wave" across the upper chest, and showed a marked pilomotor response and multiple pectoral muscle fasciculations over the upper thoracic segments when a complete penile erection was present. Stretch of the internal anal sphincter and nocuous stimulation within the genital zone intensified this sensation or, with the penis flaccid, produced a sensation identical to that associated with an erect penis. P. C. stated that he had noted "burning" of the glans penis during erection, but during examinations no such sensation was

reported. Similarly, W. M. maintained that a feeling of a " full rectum " was present when he developed an erection, but when denied visual access to the genital area failed to identify erection by this criterion.

Detectable reflex activity in the skeletal musculature of the trunk and limbs innervated by the isolated cord was never evoked by that degree of stimulation which sufficed to induce and maintain penile erection in these subjects. In the few extremely " active " patients, e.g. T. McC. and G. G., who responded to almost any innocuous cutaneous stimulation below the level of cord lesion with muscle movements, the penile receptive field for erection described above was practically the only skin area that could be touched *without* causing reflex skeletal muscle activity. The reflexogenous area for the production of extension was widened to include a portion of the genital zone in these men, for innocuous tactile stimulation of the perineum and scrotum elicited moderate extensor activity. The penis itself was not included in this receptive field, however. Thus, the application of innocuous stimuli to the penile shaft might result in erection but never caused reflex skeletal muscle activity, though, as mentioned previously, reflex flexor activity could readily be induced by nocuous stimulation of this organ.

In the remaining patients, receptive fields for the elicitation of extension did not include the scrotum or perineum despite the occasional activity resulting, apparently, from handling of the scrotum. If the thighs of the patient were widely abducted passively, it was at once evident that movement of the scrotum on the thigh was the exciting stimulus, for handling of the scrotum now evoked no reaction, and light rubbing along the inner thighs produced the activity ascribed erroneously to genital stimulation. Complete penile erection in these spinal men, therefore, was almost always exhibited in the presence of complete relaxation of the skeletal muscles innervated by the isolated cord, and the lack of reflex skeletal muscle activity appeared to be due not to inhibition, but rather to the inability of innocuous penile stimulation or the presence of erection to excite flexor and extensor activity.

The only consistent positive effect produced by penile erection was a coincidental relaxation of the scrotal dartos if that muscle was in a state of contraction. Just as contraction of the dartos and shrinkage and retraction of the penis were associated responses to nocuous and thermal (cold) stimulation within the genital zone, scrotal relaxation accompanied erection of the penis.

A number of responses were induced in 6 patients during the reflex maintenance of an erection that were not observed when the penis was flaccid; they appeared to be evokable only if erection was complete. Drawing the fingers or the prepuce firmly over the edges of the corona elicited sudden, strong tightening of the perineal skeletal musculature, and occasionally, a sudden, simultaneous and bilateral contraction of the quadriceps muscles. The former reaction was much more than a strong bulbocavernosus reflex. The entire perineal floor stiffened, and there was

a sudden, brief accession of penile rigidity. If the erected organ was not in the mid-line it was pulled sharply to that position. The same quick muscular contraction could be elicited by abruptly moving the erect penis to one side. It was frequently manifested during detumescence, the penis subsiding in a series of clonic jerks of gradually diminishing vigour. The perineal "sling" of voluntary musculature encircling and supporting the penis was evidently thrown into simultaneous reflex contraction in these men by at least two mechanisms; passive stretch of the muscles surrounding the base of the penis, and fairly forceful friction at the corona of the organ. It was interesting that the threshold at the corona for the elicitation of this response was considerably higher than the threshold for simply maintaining erection, and that no change in either threshold was apparent under conditions of prolonged stimulation.

The bilateral quadriceps contraction mentioned above was an abrupt, fleeting response noted in 2 men. In no instance did it result in more than a definite transient change in contour of the anterior thigh muscle masses. There was little or no gross movement of the limbs.

Severe generalized extensor activity produced genital activity in one patient (G. G.). Continuous maintenance of generalized extensor rigidity by tactile and proprioceptive stimuli for a period of 30 seconds resulted in erection. Though contraction of the perineal skeletal musculature was felt to be responsible for initial stages of penile swelling in this man, there was no extraneous stimulus other than brief rubbing contact of the penis with the skin of the thigh during development of complete erection. Tumescence could be induced just as rapidly, however, by local penile stimulation, and was then unaccompanied by skeletal muscle activity. Attempts to provoke or to prolong erection in the remainder of the patients by inducing extensor spasms were not successful. It was of interest, however, that a few men stated that penile erections seemed to them to be more commonly associated with extensor than flexor spasms. A rather striking finding in all men was the immediate and progressive detumescence that invariably occurred during digital (or other) stretch of the internal anal sphincter. All efforts by the men to maintain or to induce erection by penile stimulation while the sphincter was under stretch failed.

Ejaculation (as differentiated from seminal emission) was not observed in these spinal men, and, with two exceptions, none had noted its occurrence since time of injury (Table IV). The statement made by patient R. S. was of considerable interest, therefore. This man ejaculated on four occasions during 1947, under practically identical circumstances in each instance. During deep, vigorous "massage" with fingers in the suprapubic region, in an effort to completely evacuate his bladder, an unusually complete and rapid penile erection occurred (probably a result of tactile stimulation of the penis), to be followed within a few seconds by very severe generalized extensor rigidity, and simultaneous

ejaculation of what appeared to be seminal fluid[1]. The patient was especially impressed by the power of the extensor spasms accompanying ejaculation, since his involuntary movements were, at all other times, weak and incomplete. No sensation other than an intense " cold wave " across the upper thorax accompanied ejaculation.

The incidence of seminal emission is not easily estimated. Sperm were recovered from the urinary bladder of a few of these patients. Faradic stimulation of the genital tract evidently initiates, in certain instances, a smooth muscle response adequate to propel seminal fluid into the urethra[2]. If, in addition, reflex contraction of the skeletal perineal musculature occurs, the fluid may be ejaculated, as was noted in patient R. B. (Table IV).

Cremaster muscle activity was elicited in 7 of the 29 spinal men under consideration in this paper. Bulbocavernosus reflexes were present in all patients of the series who demonstrated reflex activity below the level of cord transection.

X. Tendon Reflexes and Abdominal Reflexes

Knee-jerks were obtained in 24 of 25 men, and were extremely vigorous in 16 patients. Ankle-jerks could not be elicited in 4 men, and when evoked in other subjects, were usually less marked than were responses to similar percussion of the patellar tendons. There appeared to be no correlation between the level of cord lesion and the presence, or strength, of these tendon reflexes (Table V).

Considerable differences in force of response sometimes existed between the right and left limbs in a given subject, and these differences were found to persist for long periods. Many men remarked on the differences in activity between their lower limbs, noted originally by them a few months after injury and persisting thereafter for years.

All but one patient responded to percussion of the recti abdominis muscles in each of the four quadrants, but the force of contraction was usually weak. Contraction of the superficial abdominal muscles could not be elicited in 18 men, and muscle response was restricted to a local contraction in one abdominal quadrant in 3 others.

Tendon and abdominal reflexes could not be elicited in the 4 chronically flaccid subjects.

XI. Reflex Activity of Bowels and Bladder

Nineteen of 25 men were able to initiate reflex evacuation of the bowels (Table VI). This was accomplished every 24 to 48 hours by digital stretch of the anal sphincter in 14 subjects, by insertion of a rectal suppository in the anal canal in 3 subjects, and, in 2 men, by light rubbing across the anal area. 6 patients required routine enemata. Evacuation occurred

[1] Microscopic examination of one of the specimens brought in by the patient disclosed a moderate number of sperm.

[2] Observations by Drs. Horne and Paull.

TABLE V.—TENDON REFLEXES AND CERTAIN SKIN REFLEXES IN 25 MEN WITH VERIFIED ANATOMIC TRANSECTION OF THE SPINAL CORD

Patient	*Level of cord lesion*	*Knee-jerks*	*Ankle-jerks*	*Deep abdominal reflexes*	*Superficial abdominal reflexes*	*Babinski reflex*
R. S.	D–2	4+	3+	2+ all quadrants	Upper 2+; low. absent	4+
D. K.	D–2	4+	3+	2+ all quadrants	Absent	4+
J. Dr.	D–3	lt.2+; rt.3+	lt.3+; rt.2+	1+ all quadrants	2+; absent L.U.Q.	3+
J. Z.	D–3	rt.4+; lt.3+	2+	2+ all quadrants	Absent	Absent
V. H.	D–3	4+	3+	2+ all quadrants	Absent	4+
T. McC.	D–4	4+	4+	1+ all quadrants	Absent	Absent
R. B.	D–4	rt.2+; lt.1+	Absent	2+ all quadrants	Absent	Absent
M. D.	D–5	4+	4+	2+ all quadrants	3+R.U.Q.	4+lt.; rt. 0
S. B.	D–5	2+	Absent	1+ all quadrants	Absent	2+
P. P.	D–5	4+	2+	3+ all quadrants	Absent	4+
C. S.	D–5	4+	4+	3+ all quadrants	Absent	3+
D. P.	D–5	3+	2+	1+ all quadrants	Absent	4+
J. B.	D–6	4+	Absent	2+ all quadrants	Absent	Absent
P. C.	D–6	4+	3+	2+ all quadrants	Absent	4+
H. F.	D–7	2+	2+	2+ all quadrants	Absent	4+
J. D.	D–8	3+	3+	2+ all quadrants	Absent	3+
G. G.	D–8	4+	4+	2+ all quadrants	Absent	4+
E. G.	D–8	Absent	Absent	Absent	Absent	Absent
L. D.	D–9	3+	rt.3+; lt.2+	2+ all quadrants	4+L.U.Q.	4+
J. W.	D–9	4+	4+	3+ all quadrants	Low. 2+; absent up.	4+
D. L.	D–9	4+	2+	2+ all quadrants	3+ R.U.Q.	4+
W. M.	D–10	lt.4+; rt.3+	lt.4+; rt.3+	1+ all quadrants	Absent	lt.4+; absent r
F. B.	D–10	4+	3+	Lower 1+; absent up.	Absent	3+
J. V.	D–10	lt.4+; rt.3+	rt.3+; lt.2+	2+ upper quad.	2+ upper quad.	4+
W. D.	D–12	3+	2+	2+ lower quad.	Absent	4+

within 30-40 seconds in those patients utilizing tactile stimulation alone, and was delayed in the other men for varying periods dependent upon the stage of bowel training the patient had reached. 7 patients experienced definite sensations either prior to or accompanying bowel evacuation (Table VII). These ranged from feelings of aching or "drawing" in the hypogastrium or lumbar areas to sweating, "gooseflesh," or flushing above the level of cord lesion. The same sensations could frequently be induced during examinations by digital stretch of the anal sphincter.

Functional activity of the bladder in this series of men with cord transections has been classified, in general, according to the stages elucidated by Munro (1936). 18 of 24 men possessed reflex bladders, which have been further subdivided in Table VI into controlled or uncontrolled types. The two latter terms refer to the social "dependability" of the bladder, and reflect its stage of training.

TABLE VI.—BLADDER AND BOWEL STATUS OF 25 PATIENTS WITH COMPLETE TRANSECTION OF THE SPINAL CORD

Patient	*Functional activity of bladder*	*Volume at which emptying occurred*	*Flow initiated by*	*Urethral catheter*	*Bowel control*
P. C.	Reflex (C)	10–12 oz.	Tapping	No	Tactile
J. B.	Reflex (U)	12–15 oz.	Tapping	Yes	Digital
W. D.	Reflex (C)	10–12 oz.	Straining	No	Digital
F. B.	Reflex (U)	12–14 oz.	Tapping	No	Digital
E. G.	Hypertonic reflex	5–6 oz.	Spontaneous	No	Digital
L. D.	Reflex (C)	6–8 oz.	Tapping	No	Suppository
D. L.	Hypertonic reflex	3–4 oz.	Spontaneous	No	Digital
W. M.	Hypertonic reflex	4–5 oz.	Spontaneous	No	Enemata
G. G.	Reflex (U)	8–12 oz.	Tapping	No	Suppository
J. W.	Reflex (U)	8–10 oz.	Pressing	No	Digital
S. B.	Autonomous	12 oz.	Spontaneous	Yes	Enemata
R. S.	Reflex (C)	10–12 oz.	Tapping	No	Digital
D. K.	Reflex (U)	10–12 oz.	Spontaneous	No	Digital
J. V.	Reflex (C)	10–12 oz.	Tapping	No	Tactile
J. D.	Hypertonic reflex	4 oz.	Spontaneous	Yes	Enemata
H. F.	Reflex (U)	10–12 oz.	Tapping	Yes	Enemata
M. D.	Hypertonic reflex	3–4 oz.	Spontaneous	No	Enemata
R. B.	Reflex (U)	6–9 oz.	Spontaneous	No	Digital
T. McC.	Reflex (C)	10–12 oz.	Tapping	No	Suppository
V. H.	Unknown	1–2 oz.	Spontaneous	Yes	Enemata
D. P.	Reflex (U)	10–12 oz.	Tapping	No	Digital
C. S.	Reflex (C)	10–12 oz.	Tapping	No	Digital
J. Z.	Reflex (C)	10–11 oz.	Tapping	No	Digital
P. P.	Reflex (C)	8–10 oz.	Tapping	No	Digital
J. Dr.	Reflex (C)	8–10 oz.	Tapping	No	Digital

(C) = controlled (U) = uncontrolled

Five men had hypertonic or hypertonic-type reflex bladders, one had an autonomous bladder, and one patient was difficult to classify because he had sustained extreme scarring of the bladder mucosa. Initiation of urination was termed " spontaneous " in certain men when they routinely placed a condom over the penis to channel urine into a portable rubber urinal, and thus made no attempt whatsoever to regulate voiding. The same term was applied if the patient carried a urethral catheter but kept it connected to a urinal and open at all times. It will be noted that 6 men still retained a urethral catheter.

Of the 6 subjects requiring enemata for bowel evacuation, all possessed uncontrolled bladders, 3 of which were hypertonic-type reflex, one autonomous, one uncontrolled reflex, and one bladder severely scarred by accidental instillation of glacial acetic acid. Both men who used anal tactile stimulation for bowel evacuation had well-controlled reflex bladders. 2 of the men who successfully stimulated bowel evacuation by insertion of a rectal suppository had controlled bladders, and one had an uncontrolled reflex bladder.

XII. Subjective Sensations

Eight of 25 patients showing reflex activity below the level of cord division failed to recall any sensations whatsoever referable to regions below the level of cord transection following injury. In addition, stimulation during examinations elicited no sensations in these subjects. The application of nocuous stimuli to the genital zone resulted in a sensation of burning referred to the perineum in 3 men. One patient complained of a feeling of "impending spasms," another felt an urgent desire to void, a third felt a "cold wave" across his upper chest, and a fourth described a sensation of suprapubic "tightening." In the remaining 10 subjects neither the presence of erections nor nociceptive stimulation elicited sensations.

"Burning" was the most common sensation referred by these men to areas below the level of cord lesion (Table VII). This paræsthesia was described as "warmth" in some cases, in others as "hot tingling," and certain subjects stated that it felt as if the affected part had been packed in ice and was simultaneously "numb and hot." 16 patients experienced burning of varied intensities. In 13 of this group, burning was related by the patients to prolonged pressure on some part of the paralysed body. All of these men reported that sitting in one position for several hours resulted in burning referred to the areas under pressure. The sensation generally was detected initially over the buttocks and perineum, and some subjects noted a tendency for the sensation to spread distally to the thighs, legs, and feet if corrective measures to relieve pressure were not taken. Burning was usually barely perceptible at onset, increased slowly in intensity, and disappeared gradually after pressure had been removed. The sensation appeared to be of a diffuse character whether the exciting stimulus was discrete or was broadly applied, but was not referred to the penis even when the stimulus originated from that organ. Peripheral distribution followed fairly closely a "saddle" shape that included the upper, posterior thighs, buttocks, perineum, and occasionally the scrotum. Burning was so intensified by smoking in one patient who had been a heavy smoker prior to injury that he was eventually forced to abstain from the use of tobacco. One man (J. Z.) evidenced surprising ability to localize the "source" of the burning sensation. He stated that he had experienced a constant mild burning originating from a small trochanteric ulcer ever since the latter had been denuded of epithelium, and that the application of alcohol intensified this sensation markedly. Various tests were carried out with the patient on his side and suitable precautions taken to exclude vision and other sensory clues. Saline on the raw surface evoked no comment, nor did the vigorous application of boric ointment. Within 30 seconds of the application of 70 per cent ethyl alcohol, the patient complained of increasing burning at the decubitus ulcer, the sensation reaching its peak a few seconds later. The alcohol was wiped away and the area washed with saline. Burning decreased slowly and reached its baseline intensity within another 20-30

TABLE VII.—SUBJECTIVE SENSATIONS EXPERIENCED BY 17 MEN WITH TOTAL TRANSECTION OF THE CORD

Patient	*Type of stimulus*	*Area stimulated*	*Subjective sensation*
R. S.	Nocuous	Genital zone	"Cold wave" across upper thorax, pectoral muscle fasciculations, and marked pilomotor activity (D–2 and D–3 segments)
	Innocuous (erection)	Penis	
	Stretch	Anal sphincter	
	Stretch	Bladder	
	Pressure	Buttocks and thighs	Burning over sacrum and thighs
J. D.	Stretch	Bladder	"Aching" just below the umbilicus
	Stretch	Anal sphincter	
	Pressure	Buttocks and thighs	Burning of buttocks and perineum
J. Z.	Nocuous	Genital zone	Burning of perineum
	Innocuous (erection)	Penis	Suprapubic tightening
	Pressure	Buttocks and thighs	Burning of buttocks and perineum
	Stretch	Anal sphincter	"Gooseflesh" chest, arms
	Friction	Urethral canal	Suprapubic tightening
T. McC.	Stretch	Bladder	Delayed onset of "tightening" in the left lower quadrant
	Stretch	Anal sphincter	
M. D.	Pressure	Buttocks and thighs	Burning of buttocks and thighs
S. B.	Nocuous	Plantar surface	Burning of legs and feet
P. P.	Nocuous	Genital zone	Feeling of "impending spasm"
	Pressure	Buttocks and thighs	Burning of buttocks and perineum
C. S.	Nocuous	Genital zone	Slight burning over the buttocks, perineum, and thighs
	Innocuous (erection)	Penis	
J. B.	Nocuous	Genital zone	Urgent desire to void
	Stretch	Bladder	A feeling of "fullness" in the lower abdomen
	Stretch	Anal sphincter	
	Pressure	Buttocks and thighs	"Numb" burning of buttocks and thighs
P. C.	Nocuous	Genital zone	"Cold wave" at level of lesion
	Innocuous (erection)	Penis	Burning of glans penis
	Stretch	Bladder	Ill-defined sensation of perineal warmth
	Pressure	Buttocks and thighs	
L. D.	Pressure	Buttocks and thighs	Burning of buttocks and perineum
J. W.	Pressure	Buttocks and thighs	Burning of buttocks and perineum
D. La	Stretch	Bladder	Feeling of suprapubic tightening
	Stretch	Anal sphincter	
	Pressure	Buttocks and thighs	Burning of buttocks and thighs
W. M.	Innocuous (erection)	Penis	Rectal "fullness"
	Pressure	Buttocks and thighs	Burning of toes and feet
F. B.	Pressure	Buttocks and thighs	Burning of buttocks and perineum
J. V.	Unknown	Unknown	Burning of buttocks and perineum
	Stretch	Anal sphincter	"Hot" feeling at nape of neck
E. G.	Pressure	Buttocks and thighs	Heat in buttocks, legs, toes

seconds. Application of alcohol to the intact skin near the ulcer elicited no comment. Repeated testing established unequivocally that, in this patient, there was a direct association between the application of alcohol to a decubitus ulcer and increase in severity of burning.

In no patient was discomfort sufficient to be a serious annoyance. Most men had " learned to ignore " the sensation, or to improvise methods to eliminate it. No complaints or requests for medication to relieve this particular sensation were received from the group throughout a two-year period of observation.

Stretch of the detrusor to the volume at which voiding usually occurred produced sensations in 6 men (Table VII). 5 of these subjects were able to utilize the onset of sensation as a reliable indication that the bladder required emptying. The sensation was capricious in P. C. The sensations experienced by these patients which were related to filling of the bladder lacked the quality of burning.

XIII. Discussion

The data presented in a previous paper (Kuhn and Macht, 1949) indicate that spinal man progresses, in time, through stages of spinal shock, minimal reflex activity, flexor spasms, and alternating flexor and extensor spasms, and that, eventually, he reaches a stage of predominant extensor activity below the level of cord division. 18 of 22 patients showed predominant extensor reflex activity two or more years after cord transection. The minimal atrophic changes in the skeletal musculature below the level of cord division in these 18 men offer strong presumptive evidence that there were no complicating lesions following cord transection. It would appear that *predominant extensor activity below the region of transection is the typical, uncomplicated, final outcome of such a lesion.* In contrast to this group representing the probable typical outcome of an uncomplicated transection of the cord *per se* were a total of 9 men who differed in varying degree from the usual picture. 5 patients were completely flaccid below the level of their cord transection; 2 men exhibited flexor spasms alone, and 2 showed approximately equal flexor and extensor spasms. These particular subjects will be considered below in greater detail.

Spinal shock.—Although he failed to distinguish cardiovascular shock from spinal shock, Bastian (1882, 1890) established the concept that complete transection of the human cord is accompanied by an immediate loss of deep and superficial reflexes in the paralysed part of the body. Bowlby (1890) corroborated this concept and stated further that deep reflexes fail to return over prolonged periods, but he believed that superficial reflexes may occasionally be retained from the time of injury. The first thoroughly documented treatise concerned with the immediate effect of total cord transection in men, and one that has been largely overlooked in the literature on this subject, was that of Theodor Kocher (1896). This comprehensive study of 15 patients with sudden total cord

transection subsequently verified at autopsy demonstrated clearly that, though deep reflexes are always completely abolished immediately following division of the human cord, skin reflexes and genital reflexes may persist and, in some cases, even be exaggerated. Examining traumatic cases a few hours after injury, Kocher found that priapism was of common occurrence immediately after cord division, and that frequently penile erection and more rarely ejaculation could be evoked by pressure on the suprapubic region, or by stroking the skin of the anus, perineum, or upper thigh. The same author reported the presence of an anal reflex in 6 men, a dartos tunic reflex in 2 subjects, and a cremasteric reflex in 1 individual ; all were elicited within a few hours of the transecting injury. Within twenty-four hours of the lesion, superficial abdominal reflexes were elicited in 5 men with totally transected cords. Marked contraction of the superficial and deep abdominal musculature in response to strong pressure on the testicles was another finding. A few days after injury some of the men responded to plantar pin-prick with movements of the toes. Kocher also made an interesting differentiation between priapism occurring immediately after injury, and reflex penile erection during later stages (*vide infra*).

Collier, in 1904, stated that " the anal and urethral reflexes . . . and the sphincter tone are present directly after occurrence of a total lesion . . ." but offered no data to support this contention. The classical studies of Head and Riddoch (1917) unfortunately did not include observations made immediately after cord transection, since the shortest interval after injury at which any patient was examined was four days. Riddoch stated (p. 439) that " cremasteric, dartos and bulbocavernosus reflexes were obtained in each patient except No. 4, on day of admission, so in all probability they were obtainable at an earlier date. In No. 1 they were elicited on the eleventh day . . . and before any sign of reflex activity was evident in the lower extremities and in No. 3 on the seventh day." The protocol of patient No. 1 states plainly, however, that these reflexes were not elicited eleven days after injury, nor were they seen during succeeding examinations until thirty-four days after cord transection. Confusion is multiplied by the statement elsewhere (p. 316) that : " The evidence so far as it goes shows that the reflex arcs belonging to the external generative organs recover early, earlier than extensor tendon-jerks, but not before the flexor muscles of the lower limbs or of the abdominal wall (recti abdominis) respond reflexly to appropriate stimulation." Martin and Davis (1948) state that they have observed genital reflexes and occasional flexion of the toes in response to plantar stimulation very early after complete transection of the spinal cord, but specific cases are not cited.

In the present series, though priapism was noted frequently, the protocols of patients usually failed to detail the presence or absence of specific reflex activities in the paralytic part of the body immediately following severance of the cord. In 2 cases in which examinations were made on

the day of injury and on succeeding days, a total areflexia was present a few hours after the cord had been severed. The reappearance of genital and anal reflexes in these men after division of the cord was interpreted as a sign of emerging cord activity. According to this criterion, the first evidence of recovery from spinal shock was manifest after three days and three weeks, respectively.

Available evidence indicates that total division of the human spinal cord results, in every instance, in immediate[1] abolition of tendon reflexes and in depression of certain skin reflexes below the region of transection. Reflexes associated with the generative organs and with the sphincters of the bladder and anus—the cremasteric, dartos tunic, bulbocavernosus and anal reflexes—may or may not survive unaltered from the moment of cord division. Paralysis of the bladder (and of the bowel if the transection is high) is invariably complete, and is manifested by retention of urine and by paralytic distension of the bowel. Certain abdominal muscle responses to painful stimuli may be evoked within hours of the injury. Abdominal reflexes are rarely elicited during the first few hours after the lesion has been incurred, but may appear in some instances as early as the day following injury and may then precede any movements of the toes or of the lower extremities. It seems probable, therefore, that there are considerable individual differences between men in regard to the depth of reflex depression resulting from sudden and complete division of the spinal cord. Though absolute areflexia may result and may persevere for a number of days in some individuals, others may never lose certain reflex responses, or they may regain them within minutes or hours of cord transection. In the light of these data, judgment as to the duration of spinal shock may depend upon the reappearance of reflex activity in the skeletal musculature of the abdomen or lower limbs, upon the return of vascular reflexes in the skin of the paralysed parts, or upon the manifestation of activity in the hitherto flaccid and atonic bladder. It is likely that the reappearance and perseverance of *any reflex* which had been completely abolished at the moment of cord transection is an indication of the lessening of spinal shock. In this report the appearance of toe movements has been selected as an arbitrary endpoint marking the termination of the stage of spinal shock, and the beginning of minimal reflex activity.

Adequate descriptions of 4 additional men in this series indicate that the stage of spinal shock, as defined in this manner, did not persist in them more than two weeks. The discrepancies indicated by anamnesis in the duration of spinal shock in other patients can, with reasonable certainty, be related to the considerable variation in duration of the stages of minimal reflex activity and of flexor spasms.

[1] Apparently the disappearance of the knee-jerk need not be synchronous with occurrence of the lesion. Knee-jerks have been repeatedly obtained in criminals immediately after decapitation and may persist as long as 90 seconds (Sternberg, 1893).

Minimal reflex activity.—As the profound reflex depression incident to transection of the cord begins to lift, nocuous stimulation of the plantar surfaces will elicit skeletal muscle responses in the lower limbs. In two subjects, tremulous twitching of the toes, brief flexion or extension of the hallux, and slight flexion or extension of the foot were among the earliest evidences of the onset of skeletal muscle activity after transection of the cord. Quivering side-to-side movements of the toes were observed frequently. Genital and anal responses appeared prior to, or simultaneously with, these movements in the distal aspects of the limbs.

The only stimuli effective in the production of early reflex activities were those of a nociceptive nature applied directly to plantar skin surfaces. Passive changes in the positions of the limbs and other manœuvres designed to place stretch on various muscles, i.e. all types of postural stimuli, failed during early recovery to evoke reflex muscular activity. In the case of the 2 men observed from the time of cord transection, proprioceptive stimulation was ineffective until the stage characterized by flexor muscle contraction visible throughout the entire lower extremity was reached. Even at this stage proprioceptive stimuli were inadequate to provoke strong flexion responses. The generalized, slow flexor activity described by Mettler (1948) as occurring during stages of recovery from spinal shock was not observed nor did flexor activity in any of the men of the present series follow such a pattern.

The development of flexor activity.—On the basis of data gathered on two subjects with recent cord division, and on 22 patients with transection of the cord of long duration, it is evident that flexor activity begins with movements at the distal parts of the limbs, and that reflex activity then successively involves the more proximal musculature. Progression of reflex activity in this manner was observed in 2 subjects studied from the time of cord division. Patients who had not been observed in early stages, but who had special reason to note the exact form of their first involuntary movements invariably stated that initial activity appeared in the distal parts of the lower extremities. After division of the cord in the dog and cat, a distal-to-proximal progression in recovery of skeletal muscle activity below the level of cord transection cannot be demonstrated, but a remarkably similar temporal sequence has been observed in the spinal monkey by Fulton and McCouch (1937).

Typical flexor activity.—Flexor activity could be evoked by nocuous and innocuous stimulation of the plantar surfaces, by nocuous stimulation within the genital zone, and, rarely, by severe nociceptive stimuli applied to the leg, thigh, and trunk. Cutaneous stimulation of the plantar surface was most effective in the elicitation of flexor activity. Light stroking and, occasionally, mere touch provoked, in some men, an upgoing hallux, dorsiflexion of the foot, and vigorous withdrawal of the limb. These responses were identical with those elicited in other patients only by the application of nociceptive stimulation to similar plantar areas. It

was observed, however, that in no patient was it possible to evoke withdrawal by innocuous stimulation, and then to fail to obtain a response to nocuous stimuli, though the reverse was frequently true. That portion of the plantar receptive field showing lowest threshold for all types of stimuli was usually the toe-pad and the medial plantar surface. In the genital zone, flexion rarely occurred to other than nociceptive stimulation. This zone, which encloses the genitalia and perineum, showed a special zone of still lower threshold at the penile glans and frænulum. Here pin-prick elicited delayed activity in the genital zone, to be discussed below, and reflex flexion characterized by muscle contraction more powerful in the proximal portions of the lower limbs. Gentle friction at the same point induced penile erection which was characteristically unaccompanied by reflex skeletal muscle activity, and caused simultaneous disappearance of any local response that was evident in the genital zone. Penile erection did not appear to alter the threshold of that organ for the elicitation of local or flexor muscle responses.

In the whole series of patients it was easy to predict which flexor muscles would engage in reflex activity. Riddoch (1917) listed the rectus femoris, gracilis, semitendinosus, and long head of the biceps femoris in an enumeration of muscles activated in his cases. Walshe (1914), who was the first investigator to describe in detail the human flexion reflex and to correlate it with the experimental findings of Sherrington (1910) in the dog and cat, pointed out that the lower limb of man is comparable, muscle segment by muscle segment, with the canine hind limb. His cases often demonstrated strong contraction in the medial hamstring muscles. Similar findings were noted in the spinal men. The most medial hamstring muscle, the semimembranosus, exhibited quite powerful contraction in all subjects, whereas the contraction of biceps femoris was considerably less forceful. The sartorius responded vigorously in a majority of men. It is of interest that adductor muscle contraction almost invariably accompanied flexor (and extensor) responses in the spinal men. Comparable muscles in the spinal cat and dog are relaxed reflexly during a flexion response.

Flexor movements in the usual subject were characterized by abrupt, jerking contractions and equally abrupt relaxations of specific flexor and adductor muscles of the lower limb. Responses resembled a muscle twitch in the steepness of contraction and relaxation phases. Stimulation rarely resulted in contraction of the ventral abdominal musculature or in crossed flexor contractions. The completeness of the flexor responses induced by plantar stimulation varied according to the intensity or frequency of the stimulus and the threshold of the patient, but a definite sequence of activity could invariably be demonstrated by modification of the testing procedure. Activity occurred always in a distal-to-proximal sequence, in the same manner that additional and more proximal flexor muscles were recruited during the recovery of reflex activity following spinal shock. No patient showed contraction of the hip flexors in the absence of active

hamstring contraction, and hamstring contractions rarely occurred in the absence of activity in the dorsiflexors of the foot.

Flexion evoked by nocuous stimulation within the genital zone, while always characterized by stronger contractions in the proximal than in the distal parts of the lower limbs, was further distinguished in some men by an absence of foot dorsiflexion or of toe movements. In a given subject, a flexion response that was strong and one that was weak appeared to employ approximately the same muscles. This is in harmony with the observation of Sherrington (1910) that a strong reflex flexion of a leg differs from a weak one only in being more powerful.

Abduction and external rotation of the thighs with plantar flexion of the great toes elicited by stimulation of the glans penis—the " sacral reflex " of Denny-Brown and Robertson (1933)—was never observed, nor were variants of this reflex as described by Langworthy (1937) noted in men of this series.

Extensor activity.—In the present series, cutaneous stimulation proved to be relatively ineffective in the elicitation of strong extensor activity. The stimulus *par excellence* was proprioceptive in nature, preferably in the form of abrupt, passive stretch of certain large muscle groups. It appeared that such a stimulus was afforded by the sudden, passive extension of a flexed thigh, and that this manœuvre was the basic stimulus which resulted in the most powerful involuntary movements of extension. It seems probable that the iliopsoas muscles were intimately concerned in this mechanism. One of the most striking features of extensor activity was the generalized involvement of the skeletal musculature innervated by the isolated cord. Once the extended position had been reached, rigidity appeared in all muscle groups of the limb, and frequently in the trunk below the level of cord transection. The degree of stiffening that occurred was correlated with the level of threshold. Some patients showed only a fleeting tightening while others responded by exhibiting a sustained, pillar-like rigidity. Relaxation was inevitably a slower, more " plastic " process, though it, too, affected all activated muscles simultaneously. Postural activity was sufficiently developed in a few of these spinal men to permit prolonged standing in warm water without support (Kuhn and Macht, 1948).

In spinal men, cutaneous receptive fields for extension rarely involved the ischial skin, perineum, or scrotum, but extended more or less diffusely over the anterior and posterior surfaces of the thighs, and, occasionally over the more distal surface of the trunk below the level of cord transection. In the few men in whom extensor movements were produced by innocuous scrotal or perineal stimulation, the receptive fields had widened in all directions to include the entire surface of the lower extremities, and, in addition, a major part of the trunk below the xiphoid. It is evident, therefore, that the perineal and ischial regions cannot be considered a part of the usual reflexogenous area for extension in spinal men.

Tendon and cutaneous reflexes.—It is interesting to contrast the reflexes

found by Kocher in men immediately following division of the cord and those present in other men years after cord transection. Kocher emphasized the immediate and total abolition of tendon reflexes after injury. It is apparent that, in the usual patient, tendon reflexes become hyperactive with the passage of time, and that quadriceps clonus and ankle clonus are then not uncommon findings. It seems probable that superficial abdominal reflexes, though present frequently within hours of cord division, are found only rarely in chronic spinal men and are then fragmentary—in this series, contraction of the superficial abdominal muscles was noted in only 7 men, and in 3 of them the response was restricted to one abdominal quadrant. Reflex contraction of the recti abdominis muscles in response to painful stimuli was noted by Kocher in a number of his cases soon after injury, but could be elicited in only 5 of the present series of 25 men. A strong Babinski reflex appears to be a typical response in spinal men to stimulation of the plantar surface.

Genital activity.—Within the genital zone, a special focus limited to the penile glans and frænulum was remarkable in that it was not only the area of lowest threshold for flexor responses and local genital reactions (nociceptive stimuli) but, in addition, possessed lowest threshold for penile erection (innocuous stimuli). Reflex flexion, characterized by stronger muscle contraction in the proximal parts of the limbs, was bilateral with mid-line pin-prick, and ipsilateral with deviation of as little as 2 mm. to either side of the mid-line. Local genital reaction was elicited invariably, even in the few subjects who failed to show flexion responses to genital stimulation. Reflex activities constituting the local genital reaction included bulbocavernosus and anal reflexes, succeeded usually by delayed and slow contraction of the scrotal dartos and of the penile shaft. These responses were dependent upon the frequency and intensity of nocuous stimuli and the threshold of the patient. They appeared to occur in a sequence, which depended upon the exact site of the stimulus. Maximal genital retraction was accompanied occasionally by outbursts of pilomotor and sudomotor discharge above the level of cord lesion. In these instances it is possible that the afferent impulses causing autonomic discharge above the level of cord division by-pass that level through autonomic pathways.

It is probable that the capacity for reflex penile erection may frequently be preserved from the moment of cord division. Kocher (1896) used the term priapism to designate an erection in which there is swelling of the corpora cavernosa penis but the glans penis and corpus cavernosum urethræ remain flaccid. In his cases this " priapism " was not always present nor was it always equally developed following cord transection. Of 7 patients examined by Kocher within a few hours of injury, 2 showed slight and 5 showed strong priapism. During succeeding days reflex penile erections were obtained by rubbing of the penis and other manœuvres, and were evidently complete erections of the entire organ. Recently, Martin and Davis (1948) stated that they have produced incomplete erections in some paraplegic men by strong pricking of the soles, and

describe an engorgement of the organ quite similar to the " priapism " of Kocher. One man of the present series, observed shortly after transection of the cord, exhibited vigorous erection of the entire penis for a number of hours, but the organ soon became flaccid and reflex erections could not be elicited until approximately seventy-two hours after injury and were then incomplete. Reflex erections could not be evoked in another subject until twenty-four days after division of the cord. Though capacity to show penile erection was not maintained from the moment of severance of the cord in these particular subjects, it appeared to among the first reflex responses that recover from spinal shock. In the men of this series, complete or incomplete penile erections were never observed to result from nocuous stimulation of any part of the body.

It is evident that the "coitus reflex" described by Riddoch (1917) was not observed in this series of spinal men. Cremasteric reflexes were elicited infrequently ; seminal emission was not observed ; and penile erection *per se* was never productive of reflex muscle contraction in the ventral abdominal wall or in the lower limbs. If there was any reflex activity below the level of cord transection in these men, the capacity to develop complete penile erections through non-nocuous stimulation at the glans was always present. A number of the patients married and engaged in sexual intercourse. With the exception of R. S., none had noted ejaculation since injury, and prolonged stimulation of the penis during examinations failed to provoke it. The unusual reflex skeletal muscle activity manifested by patient R. S. at the moment of ejaculation is of interest—statements of other men suggest that similar movements occurred in them during penile erections. The available evidence in this series is scanty, but indicates that the clonic extensor muscle activity noted by Müller and Dahl (1910) to accompany expulsion of seminal fluid in the spinal dog may be occasionally exhibited by spinal men. The quadriceps contraction observed to accompany strong, innocuous friction over the glans of the erect penis in 2 patients is suggestive evidence of selective extensor muscle excitation.

Semans and Langworthy (1938) have demonstrated that, in the cat, ejaculation depends upon contraction of striated muscles innervated by the internal pudendal nerve, whereas emission takes place separately in response to stimulation of the abdominal sympathetic trunks or the hypogastric nerves. Emission is defined by these workers not as expulsion of seminal fluid through the external urethral meatus, but as that mechanism whereby seminal fluid is transported from the seminal vesicles into the posterior urethra. Sexual function in the male cat, on the basis of their observations, consists of erection, emission, ejaculation, and subsidence of erection. In the light of these experimental data, convulsive tightening of the entire perineal musculature elicited by strong friction over the glans could be interpreted as the isolated ejaculatory portion of the sexual function in spinal men, occurring in the absence of emission, and, hence, failing to result in the expulsion of seminal fluid.

Though the importance of the sacral parasympathetic outflow in the mediation of penile erection has been adequately demonstrated, Root and Bard (1947) have demonstrated that complete penile erections occur regularly in male cats deprived of their sacral parasympathetic outflow when these animals become sexually excited and mount œstrous females. They traced the suprasacral erector outflow to the second, third, and fourth lumbar segments of the spinal cord, and showed that the pathway courses through the lumbar sympathetic chains and in most cases reaches the penis by way of the inferior mesenteric ganglia and the hypogastric nerves. In view of these experimental data, the human case-histories reported by Thorburn (1888), Bernhardt (1888), Muller (1901), and others, assume new significance. Each of their patients sustained traumatic injuries of the cauda equina or sacral cord, resulting in complete anæsthesia of the penis, perineum and anal regions. Despite complete insensibility of those areas after injury, the men developed penile erections in response to psychic stimuli and were capable of sexual intercourse, though the semen flowed out very slowly following copulation. In one patient seen by the author, with an injury at the level of the first lumbar vertebra, it was necessary as a therapeutic measure to sever all anterior and posterior roots below L–I. Thus, a lesion was produced similar to the experimental lesions of Root and Bard. It was noted during operation that the cord and roots above the first lumbar roots appeared quite normal. Following operation, the patient still had penile erections and the latter were associated with sexually stimulating situations. In this man there could be no question that the skin of the pelvis and genital region had been completely de-afferented, and that reflex penile erections could not be elicited. In addition, the anal reflex was absent and the bladder atonic. Therefore, it appears credible that in man penile erection may occur despite total interruption of a majority of the lumbar and all of the sacral innervations. Presumably, in the case cited, the erections were mediated by sympathetic fibres which leave the cord above L–I.

Seminal emission was noted repeatedly by Riddoch (1917) in one of his patients for many weeks after cord transection. Kocher (1896) remarks that ejaculation is of rare occurrence following division of the human cord. Seminal emission or ejaculation was not observed in the two men of the present series followed from the time of injury, and data from the series of patients with cord transection of long duration indicate that these phenomena are of rare occurrence in spinal men.

There was no significant relation between the presence of reflex cremaster muscle activity and the capacity to develop erections. Those subjects in whom a well-marked cremaster contraction could be elicited showed, in addition, quite powerful involuntary extensor activity. The association of a cremaster reflex with predominant flexor activity described by Brain (1947) was not seen.

Reflex activity of bowels and bladder.—According to the functional criteria laid down by Munro (1936), 10 men with transected cords possessed

controlled reflex bladders. Reflex bowel control in the same subjects was correspondingly well developed. In none of these men were enemata necessary. In contrast to this group, those patients who had failed completely to attain reflex bowel control possessed, in addition, uncontrolled bladders. Thus there appeared to be a fairly close correlation between the degree of reflex control of the bowel and that of the bladder in this series of spinal men.

In an effort to test the activity of the anal sphincter during maximal contraction of the detrusor, a balloon manometer was inserted into the anal canal of a number of patients, and fluid introduced slowly into the bladder. Changes in bladder pressure were recorded simultaneously with those occurring in the anal sphincter. It was found that anal sphincter tonus invariably fell markedly during a strong reflex contraction of the detrusor, and returned slowly to baseline as bladder pressure subsided. Variations in intra-rectal pressure were not recorded, but the data obtained by Denny-Brown and Robertson (1933) showed that intra-rectal pressures rose in their subjects during detrusor contractions. It is probable that, in spinal men, the reciprocal relation between activity of rectum and anal sphincter is similar to that between detrusor and external urinary sphincter. There has been adequate demonstration that the reflex evacuation of the bladder which may follow stimulation of the lower limbs is not part of a " mass reflex " but that, on the contrary, the external urinary sphincter may be immediately contracted during a flexion response (Denny-Brown and Robertson, 1933). In this instance also, the reactions of anal sphincter and external urinary sphincter are quite similar. In the reflexly active patients of this series, the application of nociceptive stimuli to either the soles or to the genital zone resulted in contraction of the anal sphincter, and, if the patient was voiding, such stimuli caused an immediate cessation of urination. Reflex bladder evacuation was precipitated by nociceptive stimulation in a few rare instances, and then only when the stimuli were applied within the genital zone. This observation is in accord with those previously made by Denny-Brown and Robertson.

Subjective sensations.—In general, the subjective sensations experienced by these patients and referred to the skin areas below cord transection were similar to those described by Davis and Martin (1947). The segmental level of lesion was, apparently, of no significance in the production of sensations. Radicular pain at the level of cord injury in one of the subjects was permanently eliminated by local procaine infiltration.

More than half of this group of spinal men experienced burning sensations of varied intensities in skin areas innervated by dorsal roots of the isolated cord. There appeared to be a fairly definite relation between prolonged postural pressures and the production of these sensations. Although psychiatric evaluation of the role played by emotional factors in the production of burning pain below cord transection was not undertaken, it does not seem likely that this sensation is explainable solely by

" personality " factors in the men. The pathways for afferent impulses which might mediate such sensations are unknown.

Reflex response to thermal stimuli.—Evidence has recently been presented by Macht and Kuhn (1948) that the isolated human spinal cord, like that of the cat, is capable of mediating responses to thermal stimuli. Spinal men who demonstrated reflex activity below the level of cord division showed no response to immersion of the distal parts of their lower extremities in water of body temperature, whereas flexion withdrawal of the limbs was invariably evoked by immersion in " cold " water. It seems probable that such responses were produced by stimulation of Krause's end-bulbs, and that the sensory modality involved was *cold*. It has been demonstrated that these responses occur in spinal men following immersion of the limb in water appreciated as cold (but not painful) by normal individuals ; that thresholds can be readily modified by prior immersion of the extremity in water of very high or very low temperature ; that asphyxia of the limbs abolishes responses to cold in a manner similar to that which occurs in normal subjects ; and, finally, that adaptation occurs rapidly, as would be anticipated with stimulation of thermal receptors. Responses elicited by immersion in " hot " water differed significantly in that they were independent of skin or blood temperature, and were produced, apparently, by stimulation of free nerve endings. It was suggested, in this instance, that the sensory modality involved was *pain*.

Mass flexion and mass extension.—In the light of the data presented, the concept of a " mass reflex " as introduced originally by Head and Riddoch (1917) needs revision. These authors described the reflex as a specific grouping of involuntary activities which can be elicited by the cutaneous stimulation of spinal men—" an excessive and widespread reflex discharge characterized by flexor spasm of the ventral abdominal wall and of the lower extremities ; evacuation of the bladder and rectum ; and sweating from an area of skin varying with the level of the lesion." Over a period of years, moreover, various interpretations have been placed on the term which disregard its original implications. Since, however, definite and predictable flexor and extensor activity patterns are exhibited by spinal men whenever they display reflex activity, and since, in addition, those patterns of activity are elicited from specific reflexogenous zones, it is apparent that certain restrictions and elaborations of the concept of mass reflex are necessary. Thus, spinal sweating and facilitation of reflex evacuation of the bowel or bladder cannot be considered components of typical flexor activity patterns in spinal men. Similarly, in so far as flexion responses alone are considered, reflex response in the ventral abdominal wall is not a usual occurrence. Reflex activity is certainly widespread, but only within the limits of the particular flexor muscle pattern of response evoked, and, in that sense, is never excessive. Specific activity patterns result in these men not from stimulation of diffuse, ill-defined areas of skin but rather from specific and

well-localized receptive fields. In view of these considerations, it is suggested that the concept of a mass reflex be applied exclusively to the combined flexor and extensor patterns of skeletal muscle activity elicitable in spinal men, and, further, that, within this concept, the terms mass flexion and mass extension are of value in the description of *two major activity patterns*. *Mass flexion* is the abrupt reflex contraction of certain specific flexor and adductor muscle groups of the lower limbs, and these muscle groups respond to plantar cutaneous stimulation in additive, distal-to-proximal sequence. Relaxation from mass flexion is characteristically rapid. Muscle contraction in the remaining paralytic musculature does not usually occur, and crossed flexor movements are rare. *Mass extension* is the reflex contraction of the entire musculature of one or both lower limbs in response to proprioceptive stimulation, converting them into rigid props, and, frequently, involving the trunk to the level of cord lesion. Relaxation from mass extension is plastic in nature. Responses do not appear to be additive, and muscle rigidity is maintained for varying periods. Mass flexion and mass extension, in addition to variation in strength, may be modified in a given subject in such a way that only fragments of the complete reflex response occur, but these fragments retain the integral pattern of the response as a whole.

Atypical outcome of cord transection.—Though there were minor variations between men in the group representing the probable typical final outcome of cord transection, major differences from the usual picture were noted in 9 subjects. 4 of these patients presented a striking neurologic picture of total areflexia, flaccid paralysis of the skeletal and rectal sphincter musculature, atonicity of the bladder, and pronounced symmetrical muscle atrophy below the level of cord division. This particular group of findings undoubtedly occurs infrequently among patients with spinal cord injuries (excluding those with total interruption of the sacral cord and cauda equina). It is unlikely that these patients remained in the stage of spinal shock for, in some cases, the condition continued as long as three years. The long-sustained total areflexia and extreme atrophic changes manifested by these men below the region of cord interruption indicated that a major deviation in the usual course had occurred and that, in addition to division of the cord, some complicating factor had altered the typical sequelæ to severance of the cord. Two explanations for the production of this neurologic condition may be entertained. The first predicates a lesion of the cord due to vascular insufficiency incident upon trauma, the second supposes a massive and generalized degeneration of peripheral nerves. Determination of the role played by one or the other, or both, of these factors will rest finally on microscopic studies of the tissues involved.

There is some experimental evidence that degeneration of peripheral nerves may be an important factor in the production of the clinical syndrome known as isolation-dystrophy. Cooper and Sherrington (1933, 1940) have called attention to marked degeneration of the sciatic nerves

in monkeys that had undergone spinal cord transection. It is not at all clear whether other nerves of the hind-limb are involved in this degenerative process (McCouch, 1924 ; Fulton and Sherrington, 1932) or that these changes can be ascribed to the effects of postural pressure. In this connexion, the total lack of response noted in one man to stimulation of the exposed sciatic nerve is of interest. A complete reaction of degeneration in muscles below the level of cord transection was obtained in 2 other patients. Hence, it is probable that total degeneration of peripheral nerves originating from the isolated cord occurred in 3 of these chronically flaccid subjects, and that the dystrophy manifested by their skeletal musculature could have resulted from these degenerations alone. The ætiology of peripheral nerve degeneration, if present in these men, is not clear. Since the postural pressures to which they were subjected after injury did not apparently differ from similar pressures exerted on those patients who subsequently developed reflex activity below the level of cord transection, it is difficult to ascribe importance to the factor of postural pressure in the production of human " isolation-dystrophy."

Among the remaining 5 subjects presenting variations from the usual neurologic picture resulting from long survival of cord transection were 2 men who showed approximately equal flexor and extensor movements two years after division of the cord. It is possible that, given sufficient time, these 2 subjects would show predominant extensor activity in the region innervated by the isolated cord. The moderate, generalized atrophy already apparent in their lower limbs was suggestive, however, of a major deviation from the usual picture. 2 other men to be considered showed even more marked changes. Both had failed to progress beyond a stage of flexor spasms, and severe selective atrophy of the extensor musculature was present in their lower extremities. Reflex activity in the extensor muscles, for some unknown reason, had either failed to develop, or had been overwhelmed at an early stage by the initial severity and rapid increase in strength of the flexor spasms. The remaining subject, though completely flaccid below cord transection, showed minimal reflex activity three years after injury. The factors involved in production of this unique neurologic status are unknown.

Miscellaneous observations.—Certain isolated observations of unknown significance have been made on these patients. Temperature changes produced a marked effect on reflex skeletal muscle activity. The decreased skeletal muscle activity resulting from immersion of the patient in warm water noted by many other authors (Bors, 1948 ; Guttmann, 1946 ; Kuhn, W., 1947) was observed also in these spinal men. Sun-bathing was a favourite pastime of many patients who had discovered accidentally the attenuative effect of an increase of body temperature on their spasms. Hyperthermia due to an infectious process, however, was not necessarily accompanied by a decrease of involuntary activity, and in some men a definite heightening in the frequency and intensity of reflex movements occurred with fever. Studies of patients with spinal cord injuries by

Guttmann (1946), Martin and Davis (1948), and Bors (1948) stress the increase of spasticity precipitated by certain infections. These observations are suggestive of the influence of chemical agents upon the thresholds of reflex activity—a subject which deserves further study. In addition, it appears that failure of involuntary skeletal muscle activity, as observed by Riddoch (1917), need not necessarily precede death from toxic febrile complications. One subject, with a *clinically* complete transection of the cord at the level of the D-5 segment, developed massive infections of the skin, entire genito-urinary tract, and, ultimately, the lungs. He maintained vigorous reflex skeletal muscle activity throughout a septic, protracted course, and severe flexor and extensor spasms of the trunk and lower extremities were still occurring a few hours before death.

XIV. Summary and Conclusions

(1) In an attempt to estimate the functional capacity of the isolated human cord, the reflex activity below the level of cord lesion was studied in 29 men with verified complete cord transection. In 27 patients, observations were possible at least two years after division of the cord, and in 2 men examinations were begun immediately after injury and were terminated approximately seven months later. Levels of cord transection ranged from the D-2 through the D-12 segments.

(2) Reflex activity below a total division of the human cord progresses, characteristically, through stages of spinal shock, minimal reflex activity, flexor spasms, and alternating flexor and extensor spasms. The majority of the men eventually reach a stage of predominant extensor activity. It seems clear that, in uncomplicated long-surviving cases of complete cord transection, predominant extensor activity below the region of injury is the typical, final outcome.

(3) Although sudden total division of the human spinal cord results in immediate abolition of tendon reflexes below the level of transection and in complete paralysis of the bladder, certain other reflexes may or may not survive unaltered from the moment of injury. In 2 subjects studied from the time of injury the period of spinal shock was characterized by a complete absence of reflex activity below the level of cord division.

(4) In 4 subjects cord transection resulted in a state of complete areflexia which lasted throughout the periods of study (two to three years). It is suggested that these results are not ascribable to cord transection *per se*, but to some complicating factor.

(5) (*a*) The earliest manifestations of flexor activity appear in spinal men at the distal parts of the limbs, and this activity then successively involves the more proximal skeletal musculature. In men responding with fully developed flexor activity, stimulation of the plantar surfaces provoked a definite additive, distal-to-proximal sequence of muscular contractions. (*b*) Although the genital zone and plantar surface each were well-demarcated areas of lowest threshold for flexor activity, nocuous

and innocuous cutaneous stimulation of the plantar surface was most effective in production of flexor activity. Within the genital zone, reflex flexion was elicited solely by a nocuous type of stimulus. (*c*) Typical flexion withdrawal was characterized by abrupt contraction of specific flexor and adductor muscles in the lower limb. Similar flexor muscles are excited in the spinal dog and cat by appropriate stimuli.

(6) Proprioceptive stimuli were most effective in the production of reflex extensor activity below the level of cord division. Sudden stretch of the iliopsoas muscle appeared to be an especially strong stimulus in the activation of generalized extension. The cutaneous receptive fields for extension in spinal men were found to extend to perineal and ischial regions only in rare instances.

(7) It is suggested that the term " mass reflex " is not adequate for the description of reflex activity in spinal men, and that the terms *mass flexion* and *mass extension* may be of value in characterizing the patterns of flexor and extensor activity elicitable below cord transection.

(8) The capacity to attain reflex penile erections was present in all men of this series who possessed any reflex activity below the level of cord transection. The focal reflexogenous zone for erection was a small area at the penile frænulum and glans ; the effective stimulus was gentle friction ; and penile erection *per se* was never productive of reflex muscle contraction in the ventral abdominal wall or in the lower limbs.

(9) Hyperactive tendon reflexes below the level of cord division, and strong Babinski reflexes in response to stimulation of plantar surfaces, were characteristic findings in the majority of these chronically spinal men.

(10) Reflex contraction of the bowel and of the detrusor usually occurred simultaneously in these subjects. The reciprocal relation between activity of the rectum and anal sphinter appears to be similar to that between the detrusor and external urinary sphincter.

(11) The isolated human spinal cord, like that of the cat, is capable of mediating responses to thermal stimuli.

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ACKNOWLEDGMENT. The author wishes to express his sincere appreciation to Dr. Philip Bard and Dr. Jerzy Rose for their advice and encouragement during the preparation of this manuscript.

LEAD IN RELATION TO DISSEMINATED SCLEROSIS

BY

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Introduction

Lead has been suggested as being the cause of many neurological symptoms apart from frank lead poisoning, and this paper deals with three aspects of the possible relationship between lead and disseminated sclerosis. These aspects are :

(*a*) The geographical incidence of disseminated sclerosis in relation to estimations of lead in soil.

(*b*) Cases of frank lead poisoning with a picture resembling that of disseminated sclerosis.

(*c*) A comparison of the estimation of the lead content of teeth in cases of disseminated sclerosis and in normal controls.

Historical

Putnam (1887) was one of the earliest writers to note the occurrence of spastic paralysis in persons who had been exposed to a lead hazard and this was emphasized again by Bechtold (1904) and Eichhorst (1913). Bramwell (1931) recorded the cases of two brothers with spastic paralysis who had been drinking from a well in which the water showed a highly toxic lead content.

Putnam had also suggested that certain cases of lead poisoning could simulate very closely the picture of amyotrophic lateral sclerosis, and Spiller (1903) found degeneration of the anterior horn cells in a case of suspected lead poisoning ; Kinnier Wilson (1907) collected several such cases. Bechtold (1904), Propper (1929) and Baker (1934) have all suggested that lead might be the cause of acute transverse myelitis.

There is no need to stress the picture of lead encephalopathy, particularly in children ; Byers and Lord (1943) found extensor plantar reflexes in these cases long after the initial lead encephalopathy had subsided. The occurrence of optic atrophy due to lead is not so well recognized. Taylor (1898) was one of the first to remark on damage to the optic nerves from lead ; and Prendergast (1910) surveyed 235 cases of lead poisoning in females, in which 75 had their eyes affected : of these 18 were totally blind, 24 partially blind and 33 had disturbed vision. Damage to isolated cranial nerves may also occur and even laryngeal palsy has been recorded by Mosny and Stern (1909) and Donelan (1913).

The diversity of the effects attributed to lead does not end here, and it is not a new conception that disseminated sclerosis may be due to lead intoxication. The foremost advocate of this theory was Cone (1934). He became interested in the subject as a result of finding lead in the cerebrospinal fluid of disseminated sclerotic patients ; this was more evident after acidosis. In some of these cases the patients had been exposed to a lead hazard. Cone emphasized the fact that lead is for the most part either excreted or deposited in the skeleton in a harmless state, but that any change in the acid-base equilibrium might cause the discharge of this stored lead into the blood, which in turn might be responsible for toxic symptoms. Cone postulated that this storage → discharge → restorage might explain the relapses and remissions of disseminated sclerosis. He suggested that this de-leading of the bones occurred when the body was subjected to the stress of pregnancy, infection or trauma, and he emphasized that attacks of disseminated sclerosis often followed precipitants of this type. McAlpine (1946) also stressed the importance of precipitating factors.

Cone found traces of lead in the cerebrospinal fluid of 7 cases of established disseminated sclerosis, and also in 1 case of epilepsy and another of polyneuritis. Rabinowitch (1933), using the same method as Cone, found that only 2 out of 27 cases of disseminated sclerosis showed lead in the cerebrospinal fluid. Bosches (1935), on the other hand, found lead in the cerebrospinal fluid of only 1 out of 16 cases of disseminated sclerosis. With the increasing sensitivity in methods of estimating traces of lead in the body, it was realized that most people have a trace of lead in their cerebrospinal fluid and that Cone's findings were not necessarily of great significance in the ætiology of disseminated sclerosis.

Tompsett and Anderson (1935) estimated lead in 20 autopsies resulting from various diseases where there had been no previous known contact with lead. They found the concentration of lead in the liver was 1·73 mg. per kilo, kidney 1·34 mg. per kilo, spleen 1·68 mg. per kilo, rib 8·55 mg. per kilo, vertebra 7·09 mg. per kilo. They also found lead in four fœtuses after four to eight months' gestation. The highest concentration of lead was found in the bones of the fœtuses, and the close relationship between lead and calcium metabolism was demonstrated by mobilization of calcium due to osteolytic processes, producing a rise in blood lead.

Kehoe (1933) had found that many foods contained lead, particularly those in tins, and Minot (1938) estimated that the average daily intake of lead was 0·2 to 0·4 mg. in America. Hansmann and Perry (1940) described 4 cases of lead poisoning in children as a result of handling lead toys. They also reported a case of a man of 63 who, having had no previous history of contact with lead, was found to be excreting appreciable quantities of lead in the urine. This patient died from a severe anæmia of unknown cause and lead content in the liver was found to be 21 mg. per 100 grammes. The lead concentration in the ribs was only 5·9 mg. per 100 grammes. They considered this showed a re-distribution

of lead and emphasized the mobilization of lead in old people. In another case they found lead in the skeleton of a premature infant and, as lead was found in the placenta, the element would be present in the fœtal skeleton if the mother's tissues contained a sufficient quantity. Lead probably behaves like calcium and passes to the fœtus in proportionate amounts during pregnancy.

Hansmann and Perry examined the lead concentration in 48 autopsies carried out on cases in which death had occurred from various conditions, and they found that the lead concentration tended to increase with age, but was rarely high under the age of 12 years. They found that the percentage of lead in the liver rose above that in the ribs in long metabolic disturbances and in pregnancy. In an analysis of fœtal lead concentrations they found 25 per cent had a really high lead content and only 38 per cent contained no lead. They concluded that lead absorption might act as an unrecognized factor in many diseases in persons in whom exposure to lead could not be traced, and that aged persons who lose calcium rapidly might be prone to lead intoxication. They emphasized that lead might precipitate maternal disease during pregnancy and might explain abortion or fœtal death, and that patients with a heavy skeletal concentration of lead might suffer lead intoxication during metabolic diseases. Finally they suggested that the development of the fœtal skeleton protects the fœtus by withdrawing lead from the circulation only when the balance of lead absorption, excretion and storage lies below a minimum toxic level.

Brown and Tompsett (1946) described acute peripheral neuritis associated with a raised concentration of lead in the blood in a case of subacute leukæmia in which leukæmic deposits had released lead from the bones; it was suggested that lead had been stored many years previously, the patient having worked as a typesetter for twelve years. Brown (1946) emphasized the general occurrence of lead even in hard water and its almost universal absorption. He found in 50 normal controls a blood lead content of 39·5 micrograms per 100 c.c., whilst in cases of metastatic malignant disease there was a mean of 91·5 micrograms per 100 c.c. in 26 patients with undue reticulo-endothelial activity the figure was 90·5 micrograms per 100 c.c. of blood. Lead will be liberated in proportion to the osteolytic process and the previous domestic hazard.

The possible association of lead toxicity has long been considered in the ætiology of swayback, a demyelinating disease of lambs. The occurrence of swayback in areas where lead had been mined made Innes and Shearer (1940) suggest it was possibly due to congenital lead encephalopathy, for it was known that lead could pass freely from the ewe to lamb across the placenta, and the lead content of brain and liver of affected animals was abnormally high. Bennetts (1937) had also considered lead as a factor in this disease until he found it could be prevented by giving copper to ewes feeding on pastures known to be deficient in copper. In Derbyshire, although the animals show a copper deficiency in their

organs, the copper content of the herbage is normal. Some factors may interfere with the absorption or utilization of copper, and lead may possibly be one of the factors.

The occurrence of a neurological condition resembling disseminated sclerosis in 4 persons doing research work on swayback made it difficult to accept a deficiency factor as the explanation, because the association appeared to be more than coincidental (Campbell *et al.*, 1947). This finding stimulated work on copper metabolism in cases of disseminated sclerosis, but so far little or no significant difference from normal controls has been found (Mandelbrote *et al.*, 1948).

Soil Lead Estimations in Relationship to the Incidence of Cases of Disseminated Sclerosis

A postal survey on the geographical incidence of disseminated sclerosis in certain counties was conducted from the Department of Neurology, Oxford during 1946.

In the counties of Cornwall, Berkshire, Buckinghamshire and Suffolk the returns showed a practically constant incidence of 2 cases per 10,000 of the population. The incidence in the Bakewell area of Derbyshire, in which swayback occurs and which is also a lead-mining area, was 5·6 per 10,000. Too much stress should not be attached to figures where the cases were not visited personally.

During this investigation a somewhat high incidence of disseminated sclerosis was noticed in the Berkshire village of C . . . . . 6 cases were reported as having occurred within five hundred yards of each other. A visit was paid to this village and the facts elicited were as follows. 5 cases were typical of disseminated sclerosis, and the sixth one of a progressive spastic paralysis. A detailed history of the cases is as follows :

Case 1.—Miss W. C.

Miss W. C. developed the disease in 1928 at the age of 22, the diagnosis being made at the National Hospital for Nervous Diseases. The patient is stated to have had retrobulbar neuritis with spastic paralysis and to have become bedridden. She died in 1935 at the age of 29.

Case 2.—Miss J. I. (Now Mrs. R.)

This patient is still living at the age of 39, and was visited personally. She was a great friend of Miss W. C. and they went to school together.

She developed symptoms of the disease at the age of 27, whilst living in Hove. These symptoms consisted of gradual loss of power in the legs, increasing blindness in one eye, and marked cerebellar ataxia. She is now 39 years old, and completely bedridden with marked mental deterioration, gross cerebellar ataxia and spastic paralysis of both legs. She has had two pregnancies, one child lived a few days only and the other pregnancy was terminated because of the disease. On the death of her husband she returned to live at C . . . . . , where she is now living. The house in which she lived as a child was extremely near that of her friend.

Case 3.—Mrs. M. L.

This patient was also at school with Cases 1 and 2, and her first symptom started at the age of 21, when she developed a numb patch on her right side which extended

from the lower ribs to the abdomen. This passed off without treatment, but during the next four years there was occasional numbness which returned over the same area for short periods. She was pregnant at the age of 25 and had no relapse then. At the age of 29 she became ill with appendicitis, and three months after the operation she began to drag her left leg, in which she noticed stiffness. A little later she started to develop giddiness and thought her right eye was at fault. At that time she lived in Ayr, Scotland, and it was there that she was diagnosed as a case of disseminated sclerosis.

At the age of 30 both legs had been severely affected, and during the next six years her condition slowly deteriorated with paralysis of the arms and legs, and she finally developed complete blindness and loss of speech. She also had had attacks of double vision and deafness. She died at the age of 36.

Her early life had been spent in C..... and she was an intimate friend of Cases 1 and 2, having gone to school with them.

Case 4.—Miss K. W.

She was aged 38 when visited, and since the age of 28 had experienced increasing difficulty in walking. She had had three attacks consistent with retrobulbar neuritis with remissions and relapses, and on examination had evidence of spastic paralysis and cerebellar disease. She went to school with the other cases, and has never left the village.

Case 5.—Mrs. K. G.

A slightly younger woman who had lived in C..... until her marriage ten years ago at the age of 24. She had never had any children.

At the age of 27, three years after her marriage, she developed weakness of the legs and some numbness in her right arm. Recently she was admitted to Colchester Hospital with the diagnosis of disseminated sclerosis.

Case 6.—Mrs. F. H.

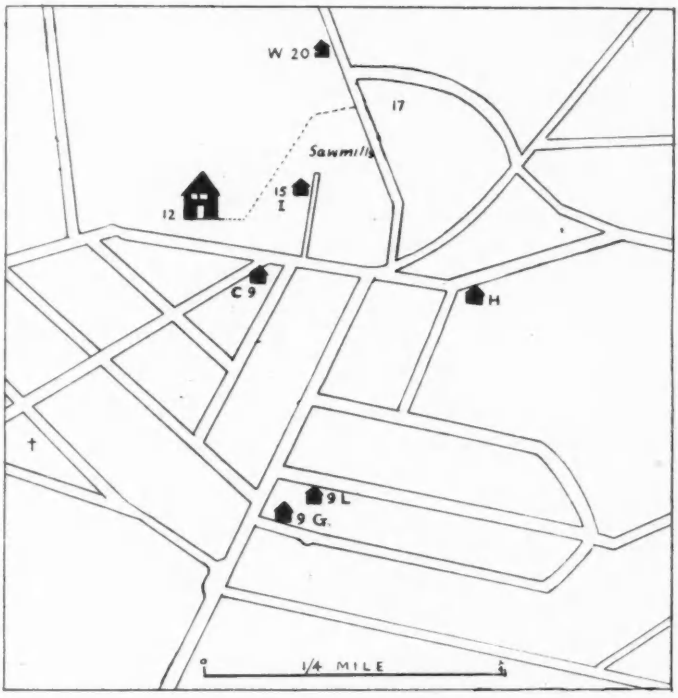
This patient, aged 57, is at present in the Woking Emergency Hospital with spastic paralysis of both legs, which was her first symptom at the age of 54. She was fully investigated at the National Hospital, where a diagnosis of disseminated sclerosis was made.

This last case is obviously not of the same classical type as the others, but has been accepted as a case of disseminated sclerosis.

The significant points of this investigation were the facts that 5 cases out of 6 attended the village school at the same time, and that 4 of these cases lived in close proximity to each other (*see* map). All had spent the first twenty years of their life in the village but the disease did not develop in two of them until they had left it. This might indicate that some common factor was responsible for the contraction of the disease in their earlier life in the village, although they showed no clinical evidence of the disease until years later.

The saw mills shown in the map have been in existence in the village for the past thirty or forty years, and the chief wood which is cut is pine, and this is indigenous to the district : pine sawdust must have undoubtedly contaminated the well water drunk by this village, but apart from this no special factors appear in the village environment except that the analysis of the soils shows them to be unduly high in lead (Table I). It is generally accepted the normal concentration of lead in soil is one to two

parts per million of soluble lead. Soil analyses showed the range to be from nine to twenty parts per million—exceptionally high figures. Certain other soils taken from the gardens of patients with disseminated sclerosis in various parts of England have shown figures of from two to



MAP C.—Showing acetic acid soluble lead estimation in soil and indicating cases of disseminated sclerosis and their houses. The figures refer to acetic acid soluble lead and the letters to cases described in the text.

thirty-two parts per million, and these are indicated in Table II. Why the lead content of the soil was so high at C . . . . . remains unexplained, but factors such as fertilization of soil and metallic dust from the electric saws must be considered. Examination of well water from the village showed no lead contamination.

TABLE I.—LEAD IN SOILS (C . . . . . .)

	Acetic acid soluble lead	*Total lead*
An	17·4 p.p.m.	150 p.p.m.
W	20·0 p.p.m.	60 p.p.m.
L	9·0 p.p.m.	60 p.p.m.
C	9·0 p.p.m.	100 p.p.m.
I	15·0 p.p.m.	70 p.p.m.

TABLE II.—LEAD IN GARDEN SOILS ASSOCIATED WITH OTHER CASES OF DISSEMINATED SCLEROSIS IN VARIOUS PARTS OF THE COUNTRY

	Acetic acid soluble lead	*Total lead*
Dundry (Somerset)	6·9 p.p.m.	—
Clapton-in-Gordano (Somerset) ..	32·0 p.p.m.	—
Brentry (Glos.)	4·7 p.p.m.	—
Whittlebury (Northants) ..	6·7 p.p.m.	—
Whitney (Oxon)	4·3 p.p.m.	—
Ca . . . . . (Glos.)		
Cases A, S and K on Map 2 ..	3·0 p.p.m.	350 p.p.m.
Case Su	4·0 p.p.m.	500 p.p.m.
Case L	3·0 p.p.m.	600 p.p.m.

These cases in Table II are all found in country districts and no town cases are included. The lead estimations are all on the high side. Lead is known to occur geologically at Clapton-in-Gordano. Swayback occurred on the farm of the case at Whittlebury. At Ca . . . the total lead was high but the most interesting factor was the grouping of cases as shown on Map 2, which can be compared with the incidence at C . . . . . .

Details of the 3 cases A, S and K are as follows :

These three cases have all lived in cottages in close proximity to each other on somewhat high ground near a quarry.

Case 1.—Mrs. A.

As far as is known she lived in the house marked A for twenty years and died in Gloucester Infirmary following an illness of about ten years' duration consisting of gradual paralysis of the legs, and attacks of numbness in the hands which was diagnosed before her death as disseminated sclerosis. She died in 1944.

Case 2.—Mrs. S., aged 47

This woman was born in the house marked S and lived there for twenty-five years. At the age of 36 she developed a transient retrobulbar neuritis in the left eye. At the age of 40 she began to develop progressive weakness of her legs with ataxia and occasional double vision. She now has advanced cerebellar ataxia and spastic weakness of both legs and the left arm. There is a pallor of the left optic disc.

Case 3.—Mrs. K., aged 22

This woman was born at the house marked K and lived there until the age of 10, then moving half a mile away until the age of 21 when she moved to the house marked K2.

At the age of 19 she noticed weakness of the hands and inability to walk, with an attack of double vision. She rapidly improved but relapsed during pregnancy two years later, with loss of vision in her right eye and a patchy loss of sensation over her thoracic region.

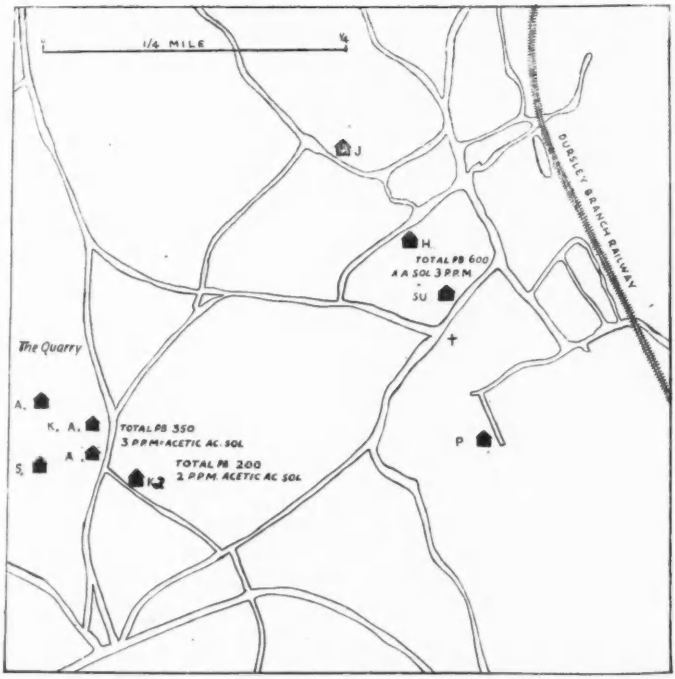
On examination she now shows a right optic atrophy, intention tremor of the left arm, thoracic sensory loss and spasticity of both legs.

COMMENTARY

These 3 cases have spent part of their life in a group of four cottages which are all isolated from the rest of the village, and had the same water supply from a well which is now walled up. As at C . . . . . there appears

to have been an undue incidence of disseminated sclerosis in a circumscribed area which is explained unsatisfactorily by coincidence alone.

Other cases of disseminated sclerosis in this rural area are also recorded on the map of Ca . . . . Since these cases have been recorded we have found a further 2 cases, resident in the country, where the lead content of the water supply was found to be higher than the accepted maximum toxic level. The first was the wife of a farmer. She had been drinking



MAP Ca.—Showing acetic acid soluble lead estimation in soil. The group of cases referred to in the text are A, K and S. Other cases of disseminated sclerosis in this vicinity are also recorded but are not described in the text.

cider with lead content of 0·5 part per million for ten years. The second was a doctor who drank well water containing lead equivalent to 0·3 part per million from 1932-1940. He was diagnosed as a case of disseminated sclerosis because he had a retrobulbar neuritis and a weakness of one leg. It is impossible to say whether this exposure to lead was a factor in these cases, but it does indicate that both water and soil may be implicated in the ætiology of the disease.

Cases of Frank Lead Poisoning With Neurological Symptoms Resembling True Disseminated Sclerosis

The following 2 cases with evidence of spinal cord damage and peripheral palsy also indicated that lead might be an element of importance in disseminated sclerosis from an occupational hazard.

Case 1.—D. P., aged 47, male

A cabinet maker, was admitted to the Radcliffe Infirmary, Oxford, in January 1946 complaining of difficulty in walking and increasing weakness of his legs.

In 1930 he noticed numbness in his hands. In 1932 his wrists became weak and he was unable to hold a knife and fork ; at the same time he had attacks of headache, diarrhœa and colicky pain. This passed off temporarily and, apart from a general weakness of his hands and wrists, he managed to continue his work until 1940, when a gradual weakness in the left foot developed. In 1944 his right leg and foot were becoming weak and stiff and in 1945 he developed loss of control of micturition and also, at times, incontinence of fæces.

In 1942 when worried about his symptoms he considered that his condition might have been due to lead poisoning. He sent a specimen of the water he was drinking to the public analyst who reported a high percentage of lead and said the water was unfit to drink due to lead contamination. Since his wife showed no symptoms he considered that the well water they were both drinking could not be responsible for his symptoms and so he went on drinking it. This water was soft and drained through peaty soil. In his work as a cabinet maker he worked for long periods with lead paint, spraying furniture, and it is possible that this could have produced lead intoxication.

On examination he walked with difficulty and had a stiff, scissored gait. The upper limbs showed bilateral weakness of both arms, wrists and fingers, weakness of opposition of the thumb and abduction and adduction of the fingers. The lower limbs showed greatly increased tone, marked spasticity with flexor spasm. Reflexes in the legs were greatly increased with clonus and bilateral extensor plantar reflexes. He had slight impairment of postural and vibration sensation.

Investigations.—A normal cerebrospinal fluid. Normal blood picture with no punctate basophilia. Normal X-rays of bone. Normal test meal. The blood lead content was 0·15 mg. per 100 ml.

Commentary

This case was admitted to hospital to exclude the possibility of a spinal tumour or disseminated sclerosis, but in view of the contact with lead both in his work and his water supply and the signs of lower motor neurone weakness in the arms with wrist drop, it was considered that the changes in the spinal cord were probably due to a lead myelopathy. Blood lead was also higher than is usually found in normal people.

Case 2.—S. C. P., aged 39, male : ex-house painter

In 1942 the patient began to notice that he was staggering about, that his arms and legs were unsteady and that the legs felt weak and heavy. He had attacks of double vision. In 1943 his symptoms were so severe and accompanied by such a degree of incontinence of urine that he became confined to bed. In 1946 he noticed weakness of his wrists and hands. Prior to 1943 he had worked for sixteen years as a house painter.

On examination he showed euphoria, nystagmus to both right and left, pallor of the right optic disc, marked cerebellar ataxia, lower motor neurone weakness of both wrists and hands, particularly of the extensor muscles of the wrists, spasticity of both legs, clonus, extensor plantar reflexes and incontinence of urine. The

only abnormality of sensation was a slight loss of postural and vibration sense in both legs.

Investigations showed a pyuria, a normal blood count and normal cerebrospinal fluid but the blood lead was raised to 0·15 mg. per 100 ml.

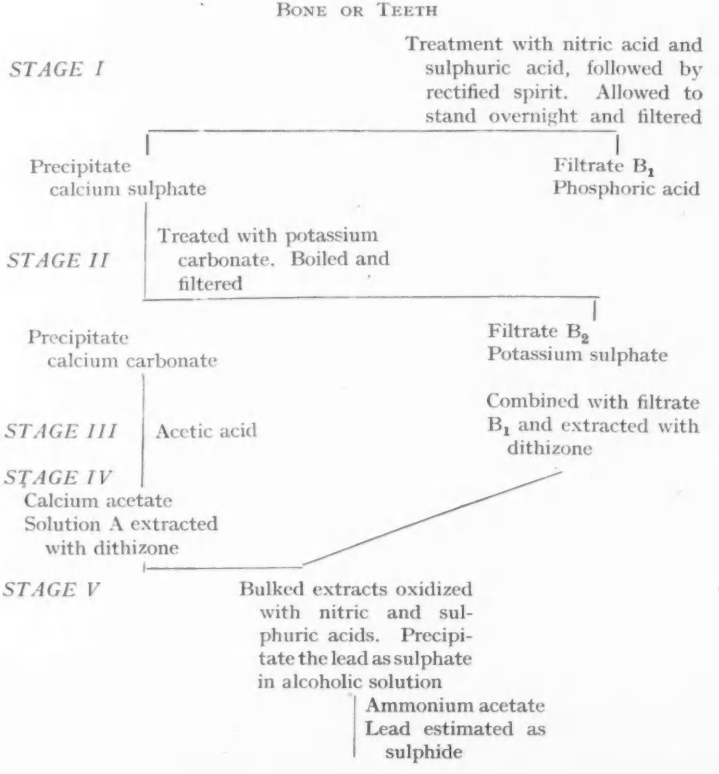
Commentary

This patient could well have been accepted as a case of progressive disseminated sclerosis but was considered to be another case of lead myelopathy due to the lower motor neurone lesion of the arms and the raised lead in the blood.

These cases are of importance as they emphasize that spinal cord damage resembling that found in disseminated sclerosis can occur in cases of known lead poisoning.

Lead in Teeth of Normal and Disseminated Sclerosis Cases

The previous work of Cone and others, and the findings of a high content in soil and water supply in relation to the incidence of disseminated


Bone or Teeth
STAGE I
Treatment with nitric acid and sulphuric acid, followed by rectified spirit. Allowed to stand overnight and filtered
Precipitate calcium sulphate
Filtrate B1 Phosphoric acid
STAGE II
Treated with potassium carbonate. Boiled and filtered
Precipitate calcium carbonate
Filtrate B2 Potassium sulphate
STAGE III
Acetic acid
Combined with filtrate B1 and extracted with dithizone
STAGE IV
Calcium acetate Solution A extracted with dithizone
STAGE V
Bulked extracts oxidized with nitric and sulphuric acids. Precipitate the lead as sulphate in alcoholic solution
Ammonium acetate
Lead estimated as sulphide

sclerosis suggested to us that it was necessary to investigate the metabolism of lead in individual cases of this disease.

The difficulty has always been to find whether the metabolism of lead was abnormal in cases of disseminated sclerosis, and any estimation of the blood and cerebrospinal fluid lead was obviously unreliable. The main storage depot for lead is in the bones, it was therefore felt the concentration being high in the teeth (Roche Lynch, 1934), that an analysis of the lead contained in the teeth of cases of disseminated sclerosis and of controls might be significant. The results have been recorded in Tables III and IV.

The method used for the determination of lead is precisely that described by Lynch, Slater and Osler (1934) and is given here in schematic form.

This procedure is essential since some 80 per cent of the lead may be present in the calcium component, with the remainder in the phosphoric acid filtrate. Care must be taken at all stages to ensure freedom from lead contamination. Blanks and controls have been made at all stages, A.R. chemicals being used throughout. The actual lead blank was consistently found to be of the order of 0·01 mg. The lead was returned as (*a*) total lead in the tooth examined and (*b*) lead in parts per million. Unfilled teeth were always selected and where possible were those without decay.

It will be seen from the tables set out (V and VI) that there is a considerable difference between the two series. Both the normal and disseminated groups were entirely unselected, although the age incidence of the disseminated cases was, as one would expect, largely between 20 and 40.

In Table IV some attempt has been made to classify the types of the disease and to show whether the residence has been mainly in town or country, a factor which we considered might influence lead absorption. Also an attempt has been made to ascertain whether cases have, in the past, been exposed to a lead hazard, and these cases have been marked by an asterisk in Table IV.

TABLE V.—NORMALS

	Tooth, Lead in Parts Per Million						
Age	1–20	**21–40**	41–60	61–80	81–100	101–140	*Total*
10–20	1	**6**					7
20–30	1	**3**	1	2			7
30–40		**9**	1				10
40–50		**2**	1	1	1		5
50–60		**2**	4	1	3	2	12
60+		**1**		2	1	1	5
	2	**23**	7	6	5	3	46

Bold figures emphasize peak of incidence.

TABLE VI.—NEUROLOGICAL CASES
Tooth, Lead in Parts Per Million

Age	1–20	21–40	41–60	61–80	81–100	**101–140**	141–200	*Above* 200	*Total*
1–20									0
20–30	1			2 (2)	1	**3**	1		8
30–40		2	2	2	4	**4**		1	15
40–50		1	(1)			**2 (2)**	1		4
50–60			1	1	1	**2**	1		6
60+						**1**	(1)		1
	1	3	3 (1)	5 (2)	6	**12 (2)**	3 (1)	1	34

Bold figures emphasize peak of incidence.

Of the cases in brackets, those in the 21-40 age-group had retrobulbar neuritis, and those in the 40-50 and 60+ age-groups are cases of spastic paralysis.

STATISTICAL ANALYSIS OF THE RESULTS OBTAINED IN THE ESTIMATION OF LEAD IN TEETH IN THE TWO GROUPS

(By G. Herdan)

(1) The two series, comprising 46 individuals in the series of normals and 34 individuals in that of disseminated sclerosis, fulfil reasonably well the requirements that the control and the disease groups should be sensibly the same in the relevant aspects of sex, age, and social class. There are 21 males and 25 females among the normals, and 15 males and 19 females among the disseminated sclerosis cases. As regards age, the series are less similar, the normal being heavily weighted in the older-age-groups, whereas the cases of disseminated sclerosis are more numerous in the younger age-groups. The influence of age on the amount of lead in teeth will be discussed in greater detail below. Here it may suffice to say that since, as is well known, the amount of lead in teeth increases normally with age, and since the normals are more heavily weighted in the older age-groups, any difference between the averages of lead for the normal and the cases of disseminated sclerosis would be still more pronounced if the age distribution was more similar. As regards social class, no selection has been taking place in this direction and each series may be regarded as a cross section of the population.

(2) It seems therefore legitimate to compare the two series with one another, as a preliminary to considering more homogeneous parts of them.

The first question to be settled is whether to base the calculations upon the absolute weight of lead, or upon the percentage weight of lead in the teeth. The latter method implies that the lead increases with the weight of the tooth, or, in other words, a positive correlation between amount of lead and weight of tooth.

The correctness of this assumption can be tested by calculating the correlation co-efficient for the dependence of lead upon weight of tooth in the disseminated sclerosis series. That co-efficient results as 0·29

and is, for the number of observations (34), not significant. This means that there is no regularity of lead increase with increase of weight of tooth. It was therefore decided to base the calculations upon the absolute lead content.

TABLE VII.—TABLE OF CONSTANTS FOR DISSEMINATED SCLEROSIS CASES (34 CASES) AND NORMALS (46 CASES)

(*Quantities in millilitres, 1 millilitre = 0·01 mg. of lead*)

	Totals	*Ratios of totals*	*Means*	*Standard deviations*	*Standard error of means*
Pb					
N	313·2	Pb/W = 4·665	6·525	3·595	152
D.S. ..	378·9	Pb/W = 7·786	11·482	6·2225	1·0832
Weight of tooth					
N	67·14		1·3987	0·5541	
D.S. ..	48·67		1·4748	0·6124	

It should be observed that the difference between the mean tooth weight in the series of normals and in that of disseminated sclerosis cases is not significant, which means that it is not the weight of teeth which could produce the difference in the mean amount of lead in both series.

The comparison of the mean lead content in the two series—6·525 for normals and 11·482 for disseminated sclerotics—gives a difference of 4·957 which, in the usual way, is tested against the standard error of such differences, resulting as 1·2, in the units chosen. Since it exceeds three times that standard error, which implies that the probability of its arising on pure chance in one and the same group is less than one in 500, it must be regarded as highly significant of a real difference between the two groups with regard to the amount of lead in teeth.

The comparison of the standard deviations in both groups justifies the same conclusion, and so does a comparison of the ratios : total Pb/ total tooth weights. The Tables V and VI (*see* pp. 62 and 63) show the distribution of the ratios Pb/W in both series ; they are clearly distinguished by the maximum frequency occurring for normals between 21 and 40 and that for disseminated sclerosis cases between 101 and 140.

(3) The above result (lack of correlation) between lead and tooth weights is interesting in itself. One of two causes, or both, may be responsible for the lack of correlation. First, the teeth may differ so widely in their state of decay in the group of the disseminated sclerosis cases that it would be sufficient to mask an existing correlation. Secondly, the accumulation of lead may here be really governed by factors other than the weight of the teeth.

Since the teeth examined were mostly unfilled, it is fair to assume that the state of decay of specimen teeth in normals was not different from

that of the disseminated sclerosis cases, and thus there should appear the same lack of correlation between lead and weight of tooth in the series of normals, provided that the accumulation of lead is governed in both cases by the same factor. Calculation, however, shows that in the series of normals there is a significant correlation between lead and weight of tooth. This shows that if there is a dependence of lead upon weight of tooth, as in the case of normals, the variation in decay does not completely obscure it. On the other hand, the total series of cases suffering from nervous diseases, comprising disseminated sclerosis cases and others, showed no significant correlation ; and the same applied, as observed above, to the series of disseminated sclerosis cases alone, though in a somewhat less pronounced way which is probably due to the small sample size of 34 observations only.

It would thus seem to follow that accumulation of lead in the disseminated sclerosis series and total series of nervous cases is due to other factors than normal metabolism of lead in teeth governing the accumulation of lead, and that the abnormal accumulation of lead in these cases must be ascribed to the one factor in which, as far as our knowledge goes, the two series are different : namely, to the incidence of multiple sclerosis or of certain other nervous diseases in the members of one group.

(4) This conclusion appears to be confirmed by a mere detailed inspection of the two series of normals and disseminated sclerosis cases. The age distribution with regard to the amount of lead in teeth is as follows :

	Normals				Disseminated Sclerotics			
Age	*Frequency*	*Per cent*		*Mean Pb*	*Frequency*	*Per cent*		*Mean Pb*
Up to 20	7	14·5	54%	4·2	—	—	—	—
30	7	14·5		6·3	7	23	68%	12·8
40	12	25·0		5·3	14	45		13·2
50	8	17·0	46%	5·8	4	13	32%	6·9
60	11	23·0		9·3	5	16		11·0
70	3	6·0		8·0	1	3		12·0
	48				31 (2 missing)			

We see first from this table that the age distributions are not quite similar. The percentages of persons up to and above 40 are for normals 54 and 46, and for disseminated sclerosis cases 68 and 32, which bears out the statement made at the beginning that the series of normals is more heavily weighted in the older age-group than is the series of disseminated sclerosis cases. This, however, has no effect upon the comparison of means because, as remarked above, greater similarity in the cases should result in an even greater discrepancy of means, since lead accumulates with age in normal cases and thus makes the average of the amount of lead per tooth rather greater in the given series of normals than it

would be in a series having the same age distribution as the disseminated sclerosis series.

Secondly, we notice from an inspection of this series of means that whereas the mean in the normal series rises with age on the whole, that for disseminated sclerosis cases does not increase with age. This may be adduced as supporting the above conclusion that the accumulation of lead in teeth in disseminated sclerosis cases is governed by other factors than those which are active in the normal cases. Just as the accumulation of lead in disseminated sclerosis cases is not governed by the weight of tooth, so it appears that it has also become independent of the age of the person.

(5) Separating the disseminated sclerosis cases according to sex gives a mean amount of lead per tooth of 11·13 for males and 11·72 for females, and thus there is no significant difference according to sex.

In the case of normals we obtain a mean of 7·30 for males and 5·68 for females which, if not amounting to a highly significant difference, may yet be considered to show some difference between the sexes in that respect (Difference 1·62, standard error of the difference 1·04.)

(6) Separating the disseminated sclerosis cases according to residence into "Town" and "Country," we get an average amount of lead of 12·008 for a town as against 9·838 for country. This gives a difference of 2·17.

The standard error of the difference is approximately of the same magnitude and the statistical significance of the difference is therefore not established. (Due partly to very small sample size per "Country" (8).)

(7) Separating the lead workers from the other disseminated sclerosis cases we obtain a mean amount of lead per tooth for lead workers of 14·683, which differs from the overall mean by 3·2 and from that of individuals not exposed to lead of 9·652 by 5·031, which in the light of the standard error of such differences must be considered significant.

(8) As regards other nervous diseases, there are 4 cases of spastic paraplegia and 2 cases of retrobulbar neuritis, which have been taken out of the total series. The retrospective mean amounts of lead are 12·2 and 12·5 as against 11·482 for disseminated sclerosis cases and 6·525 for normals. Although the numbers in these two samples are rather small, it seems justifiable to conclude that the abnormalities in the accumulation of lead which have been established by the disseminated sclerosis cases apply also to spastic paraplegia and retrobulbar neuritis.

SUMMARIZING, we may say that

(1) The average amount of lead per tooth, absolute and relative to tooth weight, in the disseminated sclerosis cases and other nervous diseases like spastic paraplegia and retrobulbar neuritis is significantly greater than the average amount in the normal case.

(2) The accumulation of the excess amount of lead does not appear

to be governed by the factors which, to some extent, determine the lead metabolism in normal persons such as weight of tooth, age and sex. This excess amount is apparently governed by factors specific to the disease.

(3) The difference in the average amount of lead per tooth in disseminated sclerosis cases which were exposed to lead for an appreciable time and other disseminated sclerosis cases, suggests that exposure to lead is one of the causes of an excessive amount of lead in teeth.

Discussion

This paper falls into three parts, each in its own way suggesting that lead may be a factor in the ætiology of disseminated sclerosis.

The somewhat high lead content of the soils at C . . . . . and the finding of an abnormal amount of lead in the water supply of certain cases indicated that a close study of the geographical incidence of disseminated sclerosis might yield some clue to its ætiology. In the two areas we have discussed there appears to have been a concentration of cases which cannot be explained by coincidence ; these cases were not related to each other and the cause of the disease may have been some common environmental factor.

Bing (1932) and Sällström (1942) have discussed the geographical incidence of disseminated sclerosis and superficially there is some similarity in the geographical occurrence of the disease to that of endemic goitre. Dean (1949) has pointed out the infrequency of disseminated sclerosis in South Africa where the soil contains little lead and a high copper content. The impression given by the study of the inconclusive papers written on the geographical incidence of the disease is that the incidence of disseminated sclerosis is high where the water supply is hard and has a high calcium content, but that lead, which is related so closely to calcium in its metabolism, may also have an effect in the production of demyelination. Wallace (1948) has informed us that lead is taken up in considerable quantities by plants which appear to be able to store it, without any toxic symptoms to themselves ; it follows that the human subject could absorb lead from vegetables which have been grown in a soil having a high lead content.

It appears that both lead and calcium may interfere with phosphorus or phospholipid metabolism in the nervous system. Shearer (1946) in a personal communication states that the inorganic phosphorus was low in lambs suffering from swayback and Bradburne and Weil (1948) have suggested that cases of disseminated sclerosis retain phosphorus which is stored in the proliferated glia cells while the phospholipids are diminished in the white and grey matter ; but the metabolism of lead, calcium and phosphorus and their effects on nervous tissue are still far from clear and radio-active studies may throw further light on this problem.

The universal risk of a lead hazard has been suggested by Brown (1946), but mere exposure to a lead hazard cannot entirely explain the damage to the central nervous system in certain cases. Two cases of spinal

cord damage due to an occupational hazard have been quoted, but a study of Table IV shows that a certain number of cases of unselected disseminated sclerosis have also had an occupation in which there has been exposure to lead. The discharge of previously stored lead into the system has been stressed by Brown, and apart from the question of disseminated sclerosis it is possible that the cases of polyneuritis associated with carcinoma of the bronchus which were recorded by Wyburn Mason (1948) may be due to lead liberated from secondary deposits in bone. Denny-Brown (1948) in reviewing the same cases in greater detail drew attention to the degeneration of the dorsal root ganglia. He noted the similarity of the histological picture to that shown in porcine ataxia described by Wintrobe (1938, 1940, 1942) which was related to a diet deficient in calcium pantothenate or pyrodoxin. Mitchell (1941) reported that the spastic ataxia occurred in pigs fed on diets of full yeast supplement and considered that this might be due to a mineral deficiency, possibly a lack of copper. It may be that minerals antagonize each other, and that lead prevents the utilization of copper by pigs, as some have suggested is the case in swayback in lambs. The occurrence of changes in muscle due to lead intoxication had been noted previously by Flury (1934) and by Aub, Fairhall, *et al.* (1925) and the picture of primary degeneration followed by cellular proliferation which they described resembles very closely the picture presented by the cases of secondary neoplastic disease described by Denny-Brown (1948). In the first case which he described, lead was found in the urine and we suggest that lead may have played a large part in the damage to muscles and neurones in his cases. Lead might well have an indirect effect on vitamin, or enzyme systems connected with trace elements ; some evidence for this has been suggested by the work of Lourac (1948) who found that in rabbits fed with lead there was a disappearance of the anti-pernicious anæmia factor ; the rapidity with which this took place indicated that lead prevented the synthesis of the factor rather than destroyed the final product. It was obvious that even in well-nourished rabbits new reserves of the factor were not produced in the animals to which lead had been administered. The enzymic nature of the intrinsic factor suggested that lead had some action on the enzyme connected with the production of this factor and interfered with cell metabolism ; other metals had no such effect. This effect of lead was very rapid and there was not time for any other toxic effect of the metal to appear.

The emphasis on cobalt being such an important constituent of vitamin B_{12} again suggests that antagonistic mineral action is present as has been demonstrated in the mineral metabolism of plants.

Putnam (1935, 1937) described thrombi in the vessels of the spinal cord in cases of disseminated sclerosis, and has suggested that venous thrombosis was the cause of demyelination : Simon and Solomon (1935) have suggested that there is a lability of the clotting time in disseminated cases, and more recently Fog and Jenson (1949) found that platelet counts

varied with the activity of the disease. Wilson and Cantarow (1944) have stated that lowering of the platelet count occurs in lead intoxication ; if, therefore, Putnam is correct in his assumption that the demyelination is secondary to vascular changes it is worth remembering that lead can also produce vascular damage and changes in the blood picture.

The suggestion that lead occurred in relation to both the environment and occupation of certain cases of disseminated sclerosis made us investigate the storage of lead in the teeth of an unselected group of cases of disseminated sclerosis, and, as has been shown in the analysis of the figures by one of us (G. H.), there is some evidence that lead is found in greater quantity and may be dealt with differently in the disseminated group. It is not suggested that lead is the only cause of disseminated sclerosis, but only that it may influence certain essential enzyme systems in certain people and produce demyelination in the central nervous system in those people.

Summary

(1) A review of the history of association of lead with diseases of the central nervous system has been made.

(2) The lead content of the soil has been studied in the homes of country cases of disseminated sclerosis, all of whom had long been resident in their villages. It was found that in the soil of one village the lead content was significantly high. The incidence of the disease in the two villages studied was abnormally great compared to findings in other areas.

(3) Lead as an occupational hazard is discussed in relation to cases resembling disseminated sclerosis.

(4) The lead content of the teeth of cases of disseminated sclerosis has been found on the average to be significantly higher than control groups.

(5) It is suggested that this evidence implies that lead does play some part in the ætiology of disseminated sclerosis. It is suggested that lead may interfere with some essential mineral, vitamin or enzyme reaction and thus precipitate demyelination. This is discussed in relation to other diseases of the nervous system.

Acknowledgments

This work developed from researches undertaken by the Department of Neurology, Oxford, while one of us (A. M. G. C.) was attached to that department, and our thanks are due to Dr. Ritchie Russell and his colleagues for the help they provided.

Our thanks are also due to Mr. Thruston of Imperial Chemical Industries, and Dr. Mitchell of the Macauley Institute, Aberdeen, for analysis of the soils and waters. Finally to the staff of the analytical Laboratory at Bristol and the many dentists who co-operated in this work.

We would also thank Professor Sir Hugh Cairns for permission to quote one case in the text.

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TABLE III.—LEAD IN TEETH

NORMALS, DISSEMINATED SCLEROTICS AND MISCELLANEOUS NORMALS

Series No.	*Lab. No.*	*Patient*	*Wt. of tooth grammes*	*Age*	*Occupation*	*Actual wt. of lead in mg. in tooth taken*	*Lead p.p.m.*
1	M.47	Miss J. H.	1·9040	18	Secretary	0·059	31·5
2	M.48	Mrs. F. T.	1·0096	27	Housewife	0·069	69·3
4	M.68	Mrs. G.	1·0100	50	Housewife	0·027	25·7
5	M.69	Mr. G.	2·2350	40	Grocery warehouseman	0·054	24·2
6	M.70	Master C. H.	0·6660	7	Schoolboy	0·019	28·5
9	M.76	Sister A.	0·9060	50	Nun	0·045	49·7
15	M.131	Mrs. B.	0·7960	35	Housewife	0·025	30·1
19	M.134	Master A. D.	1·1160	11	Schoolboy	0·045	40·3
16	M.139	Mr. R.	1·2810	50	Farmer	0·070	54·7
30	M.226	Mrs. F.	1·1760	70	Housewife	0·089	76·5
31	M.240	Mrs. P.	0·9005	44	Shopkeeper	0·065	72·2
35	M.257	Mrs. F.	0·9960	70	Housewife	0·090	90·3
36	M.258	Mrs. G.	0·6540	56	Housewife	0·053	81·6
37	M.259	Mrs. F.	1·5130	34	Housewife	0·050	33·1
38	M.260	Mr. R.	0·8040	63	Railwayman	0·060	74·5
42	M.266	Mrs. N.	1·0525	about 50	Housewife diabetic	0·100	95·1
44	M.284	Mrs. S.	1·1710	60	Housewife	0·130	111·0
46	M.286	Mr. P.	1·5260	51	Clerk	0·160	104·8
48	M.290	Mr. W.	2·5660	37	Gas fitter	0·065	25·3
49	M.291	Miss M. H.	1·4170	14	Schoolgirl	0·044	31·8
52	M.315	Mrs. F.	0·9600	45	Housewife	0·030	31·3
53	M.316	Mrs. S.	1·2840	55	Housewife	0·050	39·0
54	M.317	Mrs. B.	1·4400	37	Waitress	0·035	24·3
55	M.318	Mr. M.	1·2520	19	Surveyor	0·015	12·0
56	M.322	Mrs. H.	0·7215	31	Housewife	0·015	20·8
57	M.323	Mr. J.	1·9200	34	Clerk	0·070	36·5
58	M.327	Mrs. C.	1·0840	45	Housewife	0·045	41·5
59	M.328	Mrs. B.	1·0350	28	Housewife	0·040	38·7
60	M.356	Mr. R.	1·3490	53	Sheet metal worker	0·109	81·5
61	M.357	Mrs. C.	2·3980	58	Housewife	0·115	48·0
62	M.358	Mr. P.	1·0680	53	Electrician	0·047	44·6
63	M.359	Master L.	2·4470	14	Schoolboy	0·088	36·8
64	M.360	Mr. J.	1·9670	34	Businessman	0·095	48·3
65	M.361	Mr. R.	1·8320	36	Businessman	0·058	32·7
68	M.377	Mrs. E. S.	1·1944	17	Housewife	0·025	20·9
70	M.363	Mr. Pearce	0·9710	47	Solicitor	0·085	87·5
71	M.381	Mr. B.	1·8859	60	Labourer	0·049	26·5
72	M.382	Miss A. M.	1·1624	26	Typist	0·010	8·6
73	M.383	Mr. G.	1·9502	37	Engineer	0·070	35·9
82	M.25	Miss J. B.	1·2162	25	Box-maker	0·090	73·9
83	M.26	Mr. H. C.	1·2420	55	Blindmaker and fitter	0·150	120·9
84	M.27	Mrs. I. R.	2·4120	36	Housewife	0·048	20·3
85	M.28	Mr. W.	1·4260	26	Tobacco bond worker (previously baker)	0·070	49·0
86	M.29	Mrs. S.	1·0860	51	Housewife	0·070	64·4
44	M.30	Mr. C. D.	2·3348	27	Painter	0·070	30·0
45	M.31	Mr. W. P.	1·0970	26	Insurance agent	0·041	37·7

THE LUMBAR CEREBROSPINAL FLUID PROTEIN IN INTRACRANIAL MENINGIOMAS

BY

W. EUGENE STERN[1]

Introduction

Any method of investigation which may help the clinician towards the diagnosis of the site and nature of an intracranial tumour is welcome so long as it is without danger. Lumbar puncture in the presence of increased intracranial pressure from a space-occupying lesion is well known to be a hazardous procedure and is therefore generally avoided. In cases of intracranial tumour without pressure signs or in cases in which the diagnosis of tumour is in doubt lumbar puncture is frequently done. Whether in certain cases of tumour with increased pressure the information gained from the C.S.F. examination warrants the risk of lumbar puncture does not concern us in this paper. We have taken advantage of the fact that at the National Hospital, Queen Square, during the past twenty years lumbar puncture has been performed in a sufficient number of proved intracranial meningiomas to provide data for the present analysis. Our purpose is to present the information regarding the lumbar fluid protein values in these tumours in order to assess whatever factors may be responsible for altering the values from the normal.

Other workers have published observations upon the amount of protein in the cerebrospinal fluid in cases of cerebral tumour. These include Fremont-Smith *et al.* (1924), Fremont-Smith and Hodgson (1926), Greenfield and Carmichael (1925), Hewitt (1927), Hodgson (1928), Ayer (1928), Mandelboim (1930), Kafka (1932), Fremont-Smith (1932), Merritt (1935), Hare (1935), Glettenberg (1935), Sheller (1937), Bannworth (1937), Deane (1937), Shannon and Morgan (1944) and Phillips and Goswell (1944). None of these studies was limited to the consideration of a single tumour type, and in several instances the series was an exceedingly small one.

Material

The case records comprising the material for analysis cover a twenty-year span ending in 1949. This is a selected series of intracranial meningiomas in which the lumbar C.S.F. protein value was determined in each case prior to surgical or post-mortem confirmation and histological examination.

The group consists of 139 patients ; there are two examples of recurrent tumours giving in total 141 protein values for analysis. Among the group there was none about whose pathological type there would be any reasonable doubt. The pathological reports were all made by the members of the staff of the pathology department of the hospital, the great majority by the Director, Dr. J. G. Greenfield. All protein determinations were

[1] This paper was prepared while the author was a clinical clerk at the National Hospital, Queen Square, London (1948–1949).

made in the biochemical laboratory under the direction of Dr. J. N. Cumings using a uniform technique. This method is the trichloracetic acid technique (Mestrezat's Diaphanometric method) as described by Greenfield and Carmichael (1925). No example of mixed pathological types of tumour was used nor were cases which were complicated by other factors included (an example of such a factor being an extensive arterial thrombosis from tentorial herniation).

There was considerable variation in time between the fluid examinations and the final pathological confirmation in the cases of the series. This period extended from a matter of hours to an interval of twenty-five months. 13 cases had intervals of two months or longer, and 31 cases had intervals from four to eight weeks. Where more than one fluid examination was made within a few days the initial value was used. Where longer intervals intervened the figure from the specimen taken closest to the time of confirmation was employed (*see* Ayer and Solomon, 1926).

The youngest patient in the group was 19 years of age. The distribution of cases by decades can be seen below :

Age	*Cases*	*Age*	*Cases*
11–20	1	51–60	28
21–30	13	61–70	9
31–40	43	71–80	1
41–50	46		

Age did not appear as a factor influencing the protein level.

The classification of the cases as to anatomical site was not always easy, and a rather flexible attitude was maintained in view of the sometimes limited data afforded from operative notes and post-mortem description. In general the scheme used by Cushing and Eisenhardt (1938) was followed.

Location	*Cases*
Parasagittal anterior third	5
middle third	22
posterior third	3
Hemisphere convexity	37
Falx	11
Olfactory groove	12
Sphenoidal ridge outer third	8
middle third	1
inner third	5
Suprasellar	18
Base of middle fossa	6
Posterior fossa	5
Cave of Meckel	2
Multiple sites	2
Peritorcular	1
Lateral ventricle	1
Unclassified	2

Among the 141 protein values 108 (77 per cent) exceeded the upper limit of normal, 45 mg. per cent. 58 values (41 per cent) reached 100 mg. per cent or more.

The Present Study

We have thought that several variables should be considered in this study : (*a*) The location of the lesion ; (*b*) the length of history up to the time of fluid examination ; (*c*) the size (weight) of the tumour and (*d*) certain special features including the presence or absence of increased intracranial pressure and contact with the ventricular system.

(*a*) *Site of tumour.*—Table I was prepared to show the frequency of occurrence of the protein values in each of the major anatomical sites. It also presents the mean values for each site in which there were 6 or more observations. If we confine our considerations to these sites then it can be seen that the high average values for the " olfactory groove " and " sphenoidal ridge outer third " groups differ significantly from the lower mean values for the other sites. These other sites do not differ between themselves by more than might be attributable to chance, and larger numbers would be necessary to substantiate (or refute) the apparent differences. The table clearly shows that a normal protein value *may* come from any anatomical site, even from the two sites with significantly high averages. Also a high value can come from a very wide range of sites although according to our rather limited number of observations it is not likely to come from the " suprasellar " or " falx " sites. A normal value is found in 50 per cent of the " parasagittal middle third " cases as compared with about 20 per cent of " hemisphere convexity " cases.

If there were a general rule governing the protein content for tumours in a particular situation then the exceptions to the rule might be expected to show certain peculiarities. We have therefore studied in particular the tumours of the " olfactory groove " and " outer third of the sphenoidal ridge " which had protein values of 100 *mg. per cent or less* and the " suprasellar," " falx " and " parasagittal middle third " tumours with protein values of 100 *mg. per cent or more.* This study was made with reference to the reported occurrence in the tumour of cystic and degenerative changes, the reported vascularity of the growth and the extent of its dural attachment as compared with other tumours in like situations. The following information is forthcoming from these studies.

There were only 3 cases among the " olfactory groove " and " outer third sphenoidal ridge " groups with values below 100 mg. per cent. There were no features by which these tumours could be distinguished from the others in the same situation. Of the 18 "suprasellar" cases 3 had protein values of 100 mg. per cent or more. Save for their firm dural attachments these cases gave no clues as to the cause of the increase in protein. Among the 11 tumours of the " falx " 2 had values of 100 mg. per cent or more. Together with minor degenerative changes the only

TABLE I.—FREQUENCY DISTRIBUTION AND MEAN OF PROTEIN VALUES IN EACH MAIN ANATOMICAL SITE

Protein values in mg. per cent	*Parasagittal*			*Hemi. con-vexity*	*Falx*	*Olf. groove*	*Sphenoidal ridge*			*Supra-sellar*	*Post. fossa*	*Base mid. fossa*	*Others*	*Total*
	Ant. $\frac{1}{3}$	*Mid.* $\frac{1}{3}$	*Post.* $\frac{1}{3}$				*Outer* $\frac{1}{3}$	*Mid.* $\frac{1}{3}$	*Inner* $\frac{1}{3}$					
0–45	1	10	—	8	3	1	1	—	1	4	—	—	4	33
50–95	3	6	—	15	6	1	—	1	1	11	1	5	—	50
100–145 ..	—	4	3	5	1	3	3	—	1	3	2	1	2	28
150–195 ..	—	—	—	3	1	4	1	—	1	—	—	—	1	11
200–245 ..	—	1	—	3	—	2	1	—	—	—	1	—	1	9
250–295 ..	—	—	—	2	—	—	—	—	1	—	—	—	—	3
300–345 ..	—	—	—	—	—	—	1	—	—	—	—	—	—	1
350–395 ..	1	1	—	1	—	—	—	—	—	—	1	—	—	4
400–445 ..	—	—	—	—	—	—	—	—	—	—	—	—	—	—
450–500 ..	—	—	—	—	—	1	1	—	—	—	—	—	—	2
No. of observations	5	22	3	37	11	12	8	1	5	18	5	6	8	141
Mean protein values for groups of 6 or more cases		80·9		107·2	68·6	177·9	186·3			68·9		81·7		

suggestive finding was the extensive dural attachment of one of these cases. Of the 22 " parasagittal middle third " cases 6 had high values. There was no constant feature among these 6. Interference with the blood flow of the superior longitudinal sinus was not a factor, but we have studied a recent case not included in this series showing complete occlusion of the mid-portion of the sinus as its only remarkable characteristic. The protein of this case was 150 mg. per cent.

In these particular locations, therefore, we discovered only minor differences or peculiarities among those cases which were found to vary considerably from the general rule of protein values for their particular anatomical site.

We studied the histological reports of the cases in the locations mentioned above, and we also included for comparison and analysis all cases in the other anatomical sites which showed noteworthy histological features. From this analysis and comparison of reported histological features of the entire series we may say that in order to be significant in raising the protein value, degenerative and cystic changes apparently must be massive or perhaps must attain a certain absolute size. It was also found that it was difficult to correlate the increased protein values with excessive vascularity of the tumours, and the same may be said for the relationship between the protein values and the extensiveness of the dural attachment of the tumours. There remained a reasonable number of cases whose values exceeded the average for their groups and for which no peculiarity could be found to explain the altered protein.

The fact remains that a striking elevation of protein is the rule in tumours of the " olfactory groove " and of the " outer third sphenoidal ridge." A further notable fact is that among the "hemisphere convexity" tumours there were 14 cases with values of 100 mg. per cent or more (the average for the group was 107·2 mg. per cent). 6 of these 14 cases differed hardly at all in their situation from the group of " outer third sphenoidal ridge " tumours, and one case differed but little from the " olfactory groove " group (pre-olfactory of Henderson, 1938). These 7 cases conform therefore to the usual finding of increased protein in these two locations. There were 2 additional hemisphere convexity cases located for all practical purposes at the sylvian point with protein values of 55 and 90 mg. per cent respectively.

(*b*) *Length of history.*—If the length of history is significant in the development of an abnormal protein content one might expect a correlation with the height of the protein. It is admitted that tumours may be silent clinically for a long period and in certain locations may reach very large size before producing symptoms. The length of history does give us positive information of the minimal period of time during which the lesion in some way, directly or otherwise, may alter the protein content of the cerebrospinal fluid. Viewed from the opposite approach the long history may be the factor which permits the existence of a normal or only slightly elevated protein perhaps through some mechanism of

compensation, or because of the more deliberate, gradual alteration in the intracranial contents.

Table II indicates the distribution of cases in each site according to length of history, and Table III shows the distribution of protein values found in each history period. The lengths of history were calculated up to the time of admission to the National Hospital and not up to the time of the initial visit of the patient to his physician. There were 18 cases with a history exceeding eight years. Of these cases only one had a normal protein, and its length of history was ten years. 4 cases had histories between eight and nine years, and the remaining 13 cases exceeded a nine-year history, the longest being seventeen years. The protein of this last case was 110 mg. per cent, while the highest protein level found in this history period, viz. 450 mg. per cent occurred in a case with a history between eight and nine years. The highest value of the entire series, over 500 mg. per cent occurred in a case with a history between six and twelve months in length.

It is found on analysis that there is no significant degree of association between the protein values and the length of history.

(*c*) *Size of tumour.*—We have asked ourselves if there is any constant relationship between the size of the tumour and the protein level found. The weight of the tumour gives us a reasonable measurement of the size of the lesion. Weights were available in 73 cases. Table IV tabulates the cases both as to location and weight as well as to height of protein and weight. We have tumour weights for slightly over 50 per cent of the series and cannot make too close an analysis. However, there appears to be some association between the protein value and the weight of the tumour. Table IV shows the mean protein value for various tumour weights up to 125 grammes. We see that there is a relatively low average protein value for the smallest tumours. A peak is reached with tumours between 26 and 50 grammes after which there is a steady decline in the values.

It should be said that no significant degree of association was found between the weight of the tumour and the length of history, and therefore when the factors of weight and length of history were correlated with the protein values the only statistical relationship was that which has been described between the tumour weight and protein value.

(*d*) *Increased intracranial pressure.*—36 of our cases showed no evidence of increased intracranial pressure as manifested either by papillœdema or a lumbar manometric reading in excess of 180 mm. H_2O. (3 of these cases had a time lapse between the lumbar puncture and the pathological confirmation, and although papillœdema was not recorded in this interval it does not insure that a later pressure reading might not have shown an abnormal level.) The protein values in this group without pressure ranged from 20 to 280 mg. per cent. The average was 90 mg. per cent[1]. The average value for the entire series of 141 values was 105 mg. per cent.

[1]Recorded to the nearest multiple of 5.

TABLE II.—DISTRIBUTION OF CASES FROM EACH ANATOMICAL SITE ACCORDING TO LENGTH OF HISTORY

Anatomical site	*Length of history*											
	In months						36 *mo.* *to* 4 *yrs.*	*In years*				
	0–6	6–12	12–18	18–24	24–30	30–36		4–5	5–6	6–7	7–8	*over* 8
Parasagittal ant. $\frac{1}{3}$				1					2	1	1	
mid. $\frac{1}{3}$	2	1	3	1	5	1	3	1	1	1	1	2
post. $\frac{1}{3}$	1	1	1									
Hemisphere convexity	5	9	6	2	1	1	4	3	1	1		4
Falx	3	1		1	1	2	1			1		1
Olfactory groove	3	4	1	2					1			1
Sphen. ridge outer $\frac{1}{3}$		3		2								3
mid. $\frac{1}{3}$	1											
inner $\frac{1}{3}$				2		1	1					1
Suprasellar		3	3	1	3	3			3			2
Posterior fossa		1		1		1	1		1			
Base middle fossa	1		1		2							2
Multiple sites		1										1
Cave of Meckel	1	1										
Peritorcular										1		
Lateral ventricle												1
Unclassified	1					1						
Total	18	25	15	13	12	10	10	4	9	5	2	18

19 of the 36 cases without pressure were either " parasagittal middle third " or " suprasellar " tumours. Table I shows the mean values for each of these sites. The 7 " parasagittal middle third " cases without increased pressure had an average value of 65 mg. per cent. The 15 cases with abnormal pressure had an average value of 90 mg. per cent. In the case of the 12 " suprasellar " cases without abnormal pressure the average was 70 mg. per cent while the average of the 6 cases with increased pressure was 80 mg. per cent. It becomes evident that the cases which exhibit the increased pressure tend to be cases which have higher protein values, but it is also found that increased pressure *per se* is not essential for the elevation of the protein.

(*e*) *Contact with the ventricular system.*—4 cases may have a bearing on this question. The first case was that of a tumour arising by a pedicle from the choroid plexus, displacing the posterior half of the body of the lateral ventricle backwards and upwards ; the protein in the lumbar sac was 120 mg. per cent. A second case arose on the convexity of the hemisphere and penetrated sufficiently to protrude into the body of the lateral ventricle. There was a thin membrane of brain tissue separating the tumour mass from the ependyma. The protein was 200 mg. per cent. The third case was a hard tumour, deeply situated in the mid-line of the posterior fossa, pressing on the medulla and fourth ventricle (its relationship to the ventricular ependyma was not clear). The protein was 65 mg. per cent. The last case was also a mid-line tumour which presented just below the vermis of the cerebellum, between the tonsils. It blocked the fourth ventricle and may have arisen from the choroid plexus of the ventricle. The protein was 100 mg. per cent. Our cases are insufficient in number for any conclusions.

Discussion

(*a*) *The mechanism of increased protein ; previous hypotheses.*—The mechanism whereby a brain tumour alters the cerebrospinal fluid protein is not well understood. Mestrezat (1912) suggested that cerebral tumours might be associated with congestive and mild inflammatory changes which would increase the protein. Spurling and Maddock (1925) thought that an exudation occurred about the tumour and that the larger the tumour mass and the more intimate its contact with the C.S.F. space the more marked the chemical variation would be. According to Greenfield and Carmichael (1925) the tumour's situation, vascularity, and rate of growth were the chief factors which determined the protein increase. Fontecilla and Sepulvedar (1921) thought that any elevation of the protein depended upon the exact situation of the neoplasm and quoted Christiansen's observations on the increase of protein associated with cerebello-pontine angle tumours. Hare (1935) confirmed the uniformly high levels of lumbar protein in cases of cerebello-pontine angle tumours. He thought that it was the location rather than the type of the tumour which was the essential point. He believed the tumours in this location

acted much the same as a spinal cord tumour, blocking the connecting pathways for the circulation of fluid to the spinal subarachnoid space. Contact of the tumour with the subarachnoid space in supratentorial cases seemed a factor of importance to Fremont-Smith (1932). Kafka (1932) blamed capillary bleeding from back pressure in the blood vessels as well as transudation of blood plasma in the cases where high protein levels were found. Both Sheller (1937) and Bannworth (1937) again emphasized the importance of back pressure in the blood vessels, the veins in particular, which they thought led to transudation of blood proteins into the fluid. This phenomenon they thought was true especially in the case of meningiomas and tumours of the pons. It is not quite clear whether these authors believed the venous stasis occurred in the lesion itself or in adjacent vascular channels. After a careful study of 79 cases of cerebral tumour Deane (1937) concluded that the increase of protein which was found was due almost exclusively to increased transudation of blood plasma proteins. This, he wrote, was probably due to obstruction to venous return flow resulting from local compression of relatively non-anastomotic venous channels draining the choroid plexus. Phillips and Goswell (1944) supported Deane's thesis only for such cases in which the ventricular protein was increased as well as that of the lumbar fluid. These two workers believed that the constant feature of the cases in which the protein was elevated was a shift of the medullary axis. (In the case of supratentorial lesions it was a shift of the ventricular system, and below the tentorium it was a brain-stem shift.) They thought that such a shift interfered mechanically with the system whereby the protein is added to the fluid after the fluid has passed out of the ventricular system. Fremont-Smith *et al.* (1926), Fremont-Smith and Hodgson (1928), Greenfield and Carmichael (1925), Hodgson (1928) and Merritt (1935) agreed that involvement of the ventricular wall in supratentorial tumours might give rise to increased lumbar fluid protein, but Hare (1935) and Phillips and Goswell (1944) did not think that this was an important consideration. Fremont-Smith (1924) and (1932) believed that tumours of the fourth ventricle did not usually alter the protein level.

(*b*) *Discussion of present observations.*—The type of tumour which we have studied, the meningioma, by reason of its meningeal origin does in all instances abut against some extension of the subarachnoid space or ventricular system, but the mere contact with the cerebrospinal fluid does not appear to be sufficient in itself to cause an elevation of the lumbar protein. If we ask ourselves how the tumours become associated with an excess of protein we discover several possibilities some of which have been outlined by previous workers just discussed;

(1) Does the protein come from breakdown of tissue from degenerative or exfoliative changes in the lesion itself?

(2) Does it come from the vessels either of the tumour or its capsule and hence from the blood serum?

(3) Does it arise from increased endothelial permeability due to distortion of vascular channels remote from the tumour ?

(4) Does it reflect a degree of brain œdema which of itself must mean some alteration in the blood-brain and blood-C.S.F. barrier ?

We do not have satisfactory answers to these questions. We have found that certain tumours at the base of the brain attached to the meninges of the floors of the anterior and middle fossæ and at the pterion are seen to give a high percentage of elevated lumbar protein values. We think further that the factors of degeneration, excessive vascularity and broad dural attachment may or may not be associated with an elevated protein level. When such changes are gross there is more likely to be an elevated protein, yet certain cases show little change of this kind and are nevertheless associated with increased protein. It would seem that several factors must operate at once, and perhaps the ability of excessive vascularity or degeneration to alter the protein must depend in large part on the location of the tumour. We must still search for the reason to explain the increase in protein found even in the absence of special histological features.

Certain tumours at the base have potential or actual contact with the large lakes of cerebrospinal fluid. They also may have fairly extensive attachments to the underlying dura. Furthermore the fluid in the large lakes at the base of the brain has more direct contact with the spinal subarachnoid space than has, for example, the fluid in the spaces over the hemispheres and in the major fissures and sulci. We have noted the almost uniform elevation of protein among the " olfactory groove " cases. Here, although the lesions may have rather extensive attachments to the floor of the anterior fossa, yet the contact with the major basal cisterns terminates with the cisternæ chiasmatis and lamina terminalis. Extensions of the subarachnoid space of course occur along the olfactory tracts and along the sulci between the orbital gyri. The potential contact with the C.S.F., however, surely cannot be significantly greater than in the case of " falx " or " parasagittal " tumours unless the lesion occupies part of the middle fossa. We have no direct information concerning the role of tumours in this location in blocking the venous channels of the brain and the venous sinuses of the dura (*see* Moniz, 1937). Such venous blockage would be an attractive solution to the problem of the mechanism of the protein increase associated with these tumours. The anastomoses of the venous channels are rich, and we lack evidence of such strategic blockage as to give rise to transudation, œdema and protein increase in the C.S.F.

The increase of C.S.F. protein which we found associated with the tumours of the " sphenoidal ridge " also presents problems. The single tumour of the middle two-thirds of the ridge reached the size of the largest tumour of the series, 260 grammes, and its dural attachment was most extensive over the middle and anterior fossæ ; however, the protein in

this case was 80 mg. per cent. The "sphenoidal ridge outer third" tumours showed higher protein values, and we refer again to the inclusion in this category of 8 of the "hemisphere convexity" tumours, 6 of which showed strikingly elevated protein values. Tumours in this location are strategically placed to compromise the venous drainage by way of the large sylvian channels to the cavernous sinus. From the standpoint of contact between tumour and fluid, the large subarachnoid channel, the cisterna fossæ sylvii, running from the mid-line cisterns to the convexity of the hemisphere provides an ample expansion of the C.S.F. pathway ; and any tumour in the region of the pterion is in close proximity to this channel.

If the extent of the dural attachment together with the location in the region of the basal cisterns is at all significant then most tumours attached to the basal meninges in addition to those just mentioned should show substantially increased protein values. Included would be those of the "base of the middle fossa," those of the "cave of Meckel," and those attached extensively to the dura lining the posterior fossa. No normal protein figures were found among such cases in our series. However, only 1 of the 6 cases classified under "Base of the Middle Fossa" exceeded 100 mg. per cent. The 2 tumours of the "cave of Meckel" and the 3 tumours of the lateral recess of the posterior fossa all showed protein values greater than 100 mg. per cent.

Summary and Conclusions

We have made an analysis of 141 intracranial meningiomas in an attempt to throw light on the factors which influence the level of the C.S.F. protein as sampled from the lumbar subarachnoid sac. This study has in particular been concerned with the relationship between the anatomical site of the lesion and the protein values. Significantly higher protein values are found among the "olfactory groove" and "sphenoidal ridge outer third" cases compared with the other sites. Clearly, however, the test is not a sensitive one for the diagnosis of the site of a lesion. We have not discovered the source of the elevated protein in these cases. The factors involved are poorly understood and most probably differ qualitatively and quantitatively from one anatomical site to another.

I am privileged to acknowledge the stimulation and patient assistance of Sir Charles Symonds under whose guidance this study was made. I also wish to acknowledge with pleasure the expert advice and analysis of the statistical material by Professor A. Bradford Hill and Dr. W. J. Martin, Department of Medical Statistics, London School of Hygiene and Tropical Medicine. The Medical Committee of the National Hospital, Queen Square, was kind enough to permit the use of the material from the case file including the pathological data of Drs. J. G. Greenfield and J. N. Cumings.

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NON-PENETRATING INJURIES OF THE MEDIAN NERVE AT THE WRIST

BY

DAVID KENDALL

ISOLATED median nerve palsies have been recognized as occupational hazards in the course of a variety of trades. Oppenheim (1911) refers to the occurrence of the condition in joiners, locksmiths, milkers, cigar-makers, carpet beaters and dentists. The condition may also follow fractures of the wrist and carpus in which case the symptoms may be immediate or delayed; the delayed type was first referred to by Paget (1865). More recently, median palsy associated with fracture has been described by Moersch (1938), Zachary (1945) and Cannon and Love (1946). Among the patients described by the latter authors, were 3 for whose symptoms no ætiological factors could be found. Brain, Wright and Wilkinson (1947) described 6 patients with bilateral median nerve palsies in whom the condition appeared to arise spontaneously. Newman (1948) described 3 patients, 1 of whom had bilateral symptoms without obvious cause.

In this paper 14 patients are described; in 8 the condition was unilateral, and the nature of the trauma clear. In 6 the condition was bilateral and no very definite history of trauma was obtained from 5 of these although each of the 5 had been compelled by circumstance to commence unusually heavy household duties rather late in life.

Case 1.—Male, aged 50. Clerk. Complained of tingling and numbness of the index and middle fingers on use of the right hand, particularly on writing. For three months there had been difficulty in picking up small objects. Twenty years earlier, he had fallen and injured his right wrist. Examination showed gross wasting of the thenar eminence, with severe weakness of the abductor brevis, flexor brevis and opponens pollicis. Perception of pin-prick and light touch was impaired over the palmar surface of the thumb, first and second fingers as far as the proximal interphalangeal joints. The nails of these fingers were atrophic, and the skin dry. X-ray showed an old ununited fracture of the capitate bone with a severe secondary arthritis.

Operation (17.2.48).—The median nerve was exposed at the wrist, and the transverse carpal ligament divided. Excess of bone from the capitate bone was removed. The median nerve appeared thickened and lustreless in the carpal tunnel. One month later the sensory disturbance was no longer present and the condition of the nails had improved; there was no improvement in muscle power. Five months after operation, power had improved in the opponens pollicis, but severe wasting persisted. The patient was quite satisfied with his hand, and found no difficulty in using it.

Case 2.—A landgirl, aged 21. First seen on 6.12.48, complaining of pain and numbness in the left thumb and index finger of seven weeks' duration. For about one month before and one month after the onset of symptoms she had been engaged daily in loading straw and manure with a pitchfork, the shaft of which had at first produced a bruised sensation in the ball of the left thumb. The symptoms were worse at night, and would wake her. Examination showed a slight degree of wasting in the abductor pollicis brevis which was weak. Perception of pin-prick was impaired over the terminal phalanges of the thumb and index fingers ; pressure at the base of the palm produced paræsthesiæ in these two digits. The arm was rested in a sling for four weeks, at the end of which time the symptoms had subsided. The weakness of the abductor pollicis had decreased and sensation was normal.

Case 3.—An electric train driver, aged 50. For six months he had complained of progressive weakness of the right hand with inability to perform fine movements. Severe pain in the palm of the hand with tingling in the thumb, first, second and third fingers would wake him at night. In driving he used the " dead man's handle" a knob about two inches in diameter, spring loaded and requiring firm downward pressure of the palm of the hand to operate it. Examination showed severe wasting of the thenar muscles with complete loss of power in the opponens and abductor brevis pollicis muscles. There was loss of perception of pin-prick and light touch over the whole of the volar surfaces of the thumb and first three fingers, and the distal third of the dorsal surfaces. The skin of these fingers was dry and the nails atrophic. Exploration of the median nerve was considered, but it was decided first to try the effect of rest. The wrist was immobilized in a light plaster cast, leaving the fingers free and finger movements were encouraged. At the end of six weeks the sensory disturbance had almost disappeared, and there was no complaint of pain. At the end of four months, voluntary power was returning to the affected muscles and the thenar wasting was less marked. At the end of six months only very slight wasting was present, power was normal, and he was allowed to return to work after being supplied with a reinforced pad and strap to protect the wrist and base of the palm. Three months later he was free from symptoms.

Case 4.—A carpenter, aged 35, was seen on March 22, 1948, complaining of numbness and deadness of the thumb, first and second fingers of the right hand of one month's duration. The symptoms were most marked at night, and interfered with sleep. The tingling was also present when cycling, or gripping a plane or screwdriver. He returned to his civilian occupation three months previously, having had four years' Army service. There had been no injuries to the wrist or hand. Examination showed moderate wasting and weakness of abductor pollicis brevis on the right ; the remaining intrinsic muscles were normal. There was atrophy of the terminal pulp of the index finger, and the skin of the thumb, index and second fingers was dry and faintly cyanotic. The nails were normal. There was dulling of perception of pin-prick over the tips of the thumb and index finger. A light plaster cast was applied to the wrist, leaving the fingers free and three weeks later all symptoms had disappeared, no trophic disturbance was visible and sensation was normal. Wasting was still present in abductor pollicis brevis. Two months later, the wasting was just perceptible, but the hand was otherwise normal. The patient was allowed to return to work with a leather and rubber pad over the base of his palm, and was free from symptoms when seen in September 1948.

Case 5.—A man, aged 69, complained in December 1948 of numbness and loss of use of the right hand of twenty years' duration. He had been employed at a waterworks for forty years, work which involved the frequent pulling and pushing of levers with the right hand. The condition had commenced insidiously, with tingling in the thumb, first, second and third fingers, and was most noticeable at night. The hand had gradually become weaker and ability to perform fine movements was lost. The affected digits became numb, but were frequently painful

and blue in cold weather. For five years there had been intermittent ulceration of the thumb, first and second fingers, infection leading to the loss of the terminal phalanx of the second finger had occurred. Examination showed that the skin of the palm and all fingers except the fourth was dry, cold and atrophic. The nails of the first and third fingers were grossly deformed, that of the thumb lacked normal lustre, and that of the fourth finger was normal. There was a granulating ulcer on the volar and radial surface of the middle phalanx of the index finger. The thenar eminence was moderately wasted, abductor pollicis brevis being the most affected muscle, and this muscle was completely paralysed. Weak power was present in opponens pollicis. There was complete cutaneous anæsthesia over the volar surfaces of the three radial fingers and the thumb, and on the dorsal surfaces of the terminal phalanges. Postural sense was lost in the index finger. Wrist movements were normal, and there was no local tenderness.

Case 6.—A married woman, aged 43, was seen on December 8, 1947, complaining of pain in the left thumb, first and second fingers of four months' duration. Symptoms started with numbness in the tip of the index finger followed by pins and needles and aching. Symptoms were always present but were worse at night. The patient was left-handed, and undertook much heavy housework, laundry and floor-scrubbing. Examination showed atrophy of the terminal pulp of the thumb, first and second fingers with cyanosis and lack of lustre in the nails, which latter were said to grow much more slowly than those on the right. Slight wasting was present in the thenar eminence, and there was moderate weakness of opponens and flexor brevis pollicis. There was dulling of perception of pin-prick over the terminal phalanges of the affected fingers. A light plaster was applied from mid-forearm to mid-palm. When seen three weeks later, the sensory disturbance was no longer present, and normal nail growth had commenced. The plaster was removed and the patient warned not to use the hand for any heavy work. On April 26, 1948, the hand appeared normal, although there was still a very slight weakness of the thenar muscles. There were no trophic or sensory changes. When seen on June 26, 1948, the hand was normal.

Case 7—A woman, aged 19, employed as a stable hand, was seen on March 22, 1948, complaining of nocturnal tingling and numbness of the right thumb and two radial fingers for three weeks. The hand was a little clumsy, and she was unable to knit. Her occupation involved using a wooden-handled horse brush which was applied with a patting movement, and which pressed heavily on the base of the right palm. On examination no trophic changes were seen, there was wasting and weakness in the abductor pollicis brevis ; opponens and flexor brevis pollicis were normal. Perception of pin-prick and light touch were impaired over the two terminal phalanges of the first and second fingers. The wrist was immobilized in plaster for three weeks, by which time she was free from symptoms. Examination on April 26, 1948, showed no abnormality other than persistence of the slight thenar wasting.

Case 8.—A housewife, aged 28, was seen on January 28, 1949, complaining of tingling and deadness in the right index and middle fingers of two months' duration. The symptoms were constantly present, but were aggravated by scrubbing or laundry. She also noted that prolonged dorsiflexion of the wrist produced pins and needles in the affected fingers. Examination showed cyanosis of the thumb and index fingers, the skin of which was dry, and the nails dull and atrophic. There was weakness, without wasting, of the opponens and flexor brevis pollicis, and perception of pin and light touch was impaired over the distal two phalanges of thumb, first and second fingers. Plaster was applied from the mid-forearm to the mid-palm, and three weeks later the cyanosis had disappeared, the nails were growing at normal rate, and the disturbance of sensation was confined to the thumb. The slight weakness persisted. The plaster was removed and a sling was substituted, the patient

being warned against strenuous use of the hand. On February 21, 1949, no definite abnormality could be detected other than weakness of the short abductor of the thumb.

Of the 8 patients with unilateral median nerve lesions described, only 2 (Cases 1 and 5) had signs of complete interruption of conduction. The first of these 2 had a wrist injury of long standing, and the second patient had subjected his hand to repeated trauma over a very long period. The remaining 6 patients had median palsies of relatively slight degree; the symptoms nevertheless constituted a considerable disability. In each of these 6 instances the condition had followed the prolonged handling of implements in everyday use, and with one exception (Case 2) the patients were unaware of any injury being inflicted by the implement in question. In each case sensory symptoms were prominent, motor symptoms were variable and on the whole slight. Of the signs present, the tendency for the abductor pollicis brevis to be more severely affected than the other thenar muscles is noteworthy, and the occurrence of vasomotor or trophic changes in 6 of the 8 patients is striking. In this connexion it is of interest to compare the incidence of trophic disturbance in non-penetrating injuries of the type described here with their incidence in penetrating injuries. Of 600 peripheral nerve injuries examined by the writer during the recent war, there were 61 injuries to the median nerve at varying levels. Vasomotor or trophic changes were present in 46 of these and did not bear any relationship to the site of the lesion or to the presence of a concomitant injury to blood vessels. There was, however, a definite relationship between the severity of sensory and trophic changes. The latter were present in every instance where there was complete cutaneous anæsthesia in all or part of the median territory, and in approximately 75 per cent of those injuries which were incomplete, but which were characterized by more or less severe sensory disturbance. By contrast, in those injuries in which motor signs predominated, of which there were 5, only 2 showed trophic disturbance, and this was confined to atrophy of the terminal finger pulp and dryness of the skin. It was further noticed that recovery of the trophic changes tended to follow sensory rather than motor recovery. It is perhaps of interest that only two of this series of patients with injury to the median nerve suffered from causalgia; in both cases trophic and sensory changes far exceeded the motor disturbance present.

The anatomical factors in the production of median nerve palsy by pressure are considered after the account of the patients in whom bilateral palsies were present.

Case 9.—A cook-housekeeper, aged 52, was seen on March 10, 1947, complaining of pins and needles in the right hand for two years, and in the left for eighteen months. The onset was gradual and symptoms were first noticed when riding a bicycle, later becoming more constant and particularly severe at night. The patient was right-handed but was accustomed to lifting heavy pans and using a scrubbing brush with both hands. Examination showed the presence of severe wasting of

the thenar eminences, more marked on the right side, and more obvious in the lateral part of each eminence. Voluntary power was absent in the abductor pollicis brevis of each side, and opposition was weak. There was dulling of perception of pin-prick over the distal two-thirds of the volar surfaces of the first and second fingers and over the distal half of the thumbs. Light touch was normally perceived, and there were no trophic changes. Percussion over a point about one inch distal to the lower crease of the wrist produced tingling in the tips of the affected fingers. Wrist movements were full and free. There was no evidence of cardiovascular disease. At operation on March 26, 1947, the right median nerve was exposed by a longitudinal incision up to a point 3 inches proximal to the transverse carpal ligament. The nerve appeared enlarged at the upper border of the ligament, and gangliform in shape. The ligament was divided, and the nerve found to be surrounded by tough connective tissue. The nerve appeared pink in the tunnel, and the arteria comes were clearly visible. Measurements of the nerve were as follows: in the carpal tunnel 6 mm., at the upper border of the carpal ligament 7 mm., 2 inches above the ligament 4 mm. Fourteen days after operation, tingling in the fingers had ceased, and the objective sensory disturbance was less marked. Six months after operation, sensation was normal, voluntary contraction was present in abductor pollicis brevis, and opposition was normal. The muscular wasting was less marked. At this time, the wasting of the left hand appeared to have become more marked. On January 14, 1948, a similar operation was performed on the left side, and the findings were the same as on the right. In addition the nerve had a somewhat granular appearance in the carpal tunnel. On July 8, 1948, the right hand appeared normal apart from minimal wasting, and sensation was normal on the left. When last seen in October 1948, both hands were normal functionally, only slight wasting persisting.

Case 10.—A housewife, aged 53. First seen on July 3, 1948, complaining of uselessness of both hands. Symptoms had commenced in the right hand seven years previously with tingling in the thumb and index fingers, particularly in the early morning. There had been an increasing difficulty in performing fine movements, and, latterly, a tendency to drop small objects from the hand. The left hand had been similarly affected for three or four years. During the war years she had undertaken much heavy housework, including scrubbing and laundry, and also did heavy gardening. Examination showed severe atrophy of the right and left thenar eminences with complete loss of voluntary power in the short abductor and opponens muscles. There were marked trophic changes present in the thumb and index fingers, with cyanosis, dry scaly skin and nail atrophy. There was complete cutaneous anæsthesia over the distal halves of the thumbs and index fingers, and postural sensibility was impaired in the terminal phalanx of the right index finger. Wrist movements were full and free, and there was no cardiovascular disease. At operation on July 6, the right transverse carpal ligament was completely divided. The median nerve appeared somewhat smaller in the carpal tunnel than at the upper border of that structure, but appeared quite normal in colour. When seen in September 1948 the trophic and sensory changes were no longer present. Muscular wasting and paralysis were unchanged. In December 1948 power of opposition of the thumb was returning. A similar operation is shortly to be performed on the left side.

Case 11.—A housewife, aged 52. First seen on November 20, 1947, complaining of numbness of the thumb, first and second fingers of each hand. Symptoms had commenced five years and four years previously in the right and left hands respectively. The tingling was worse at night and disturbed sleep. There was difficulty in carrying out fine movements and in knitting or sewing. As a result of altered circumstances during the war, this patient had undertaken much heavy household work and gardening to which she was unaccustomed. On examination there was

severe wasting of the thenar eminences, with complete paralysis of the short abductor and opponens muscles ; the short flexors of the thumbs were weak. There was dulling of perception of pin-prick and light touch over the tips of the thumbs, first and second fingers. There were no trophic changes other than some dryness of the affected digits. At operation on December 12, 1947, the left transverse carpal ligament was divided. The median nerve appeared of normal size and texture in the carpal tunnel but appeared to be enlarged at the upper border of that structure. She was readmitted to hospital on March 9, 1948. At this time the sensory loss on the left side had disappeared and there was no longer any complaint of tingling on this side. Weakness and wasting were unchanged. On March 11, the right transverse carpal ligament was divided, and the appearance of the nerve was normal. On October 14, 1948, sensation was normal in both hands, and opposition of the thumbs was quite strong. There was some return of power in the left abductor brevis, and the muscular wasting was less marked. The patient was able once again to knit and sew and was doing all her normal housework.

Case 12.—A housewife, aged 49. First seen on December 10, 1947, complaining of wasting and weakness of the right hand for five years, and similar affection of the left hand for two years. Symptoms commenced with numbness in the tips of the right thumb and first finger. This was more marked at night and on exposure to cold. The hand had become progressively more useless. The left hand was similarly but much less severely affected. This patient had undertaken much heavy housework and gardening following the death of her husband in 1939. Examination showed marked wasting of the right thenar eminence with complete paralysis of the opponens and flexor brevis pollicis. The skin of the affected fingers was dry, the nails atrophic and there was atrophy of the terminal finger pulp. Well-marked Raynaud's phenomenon was induced by immersing the right hand in cold water for five minutes. The wasting was less severe on the left side, but with considerable loss of power in the abductor pollicis brevis. On both sides there was complete cutaneous anæsthesia over the terminal phalanges of the thumbs and first fingers, with hypoæsthesia over the middle phalanges. At operation on January 16, 1948, the right transverse carpal ligament was divided. The median nerve appeared thickened and granular at the proximal border of the ligament, but was normal in the carpal tunnel. On March 8, 1948, sensation had returned and was normal. The nails were growing more rapidly, and Raynaud's phenomenon could no longer be induced. On June 14, there was weak contraction present in the opponens and abductor muscles and the wasting was less obvious. On November 17 good contraction was present, but moderate wasting persisted.

Case 13.—A farmer, aged 40. Seen on April 5, 1948, complaining of pain and pins and needles in both hands for two years, and wasting of the hands for one year. The symptoms were worse after use of the hands and were pronounced at night. His work involved much heavy lifting and he spent a considerable time driving a tractor and operated the controls with both hands. The levers operating the various implements required considerable effort to move them, and steering the tractor necessitated a firm grip on the wheel. Examination showed moderate wasting of both thenar eminences, with marked weakness of the short abductor muscles and moderate weakness of opposition of the thumbs. Perception of pin-prick and light touch was impaired over the first, second and half the third fingers and over the volar surfaces of the thumbs. The nails of the affected fingers were atrophic and the skin dry. At operation both transverse carpal ligaments were divided. The median nerves appeared of normal size, but the nerve sheaths lacked normal lustre. Two weeks after operation the sensory symptoms had disappeared, and only minimal loss could be detected to pin and light touch. Six months after operation he was reported to have normal voluntary power in the affected muscles and to be using his hands normally. He was not seen by the writer at this time.

Case 14.—A housewife, aged 46. First seen on February 12, 1948, complaining of wasting and numbness of both hands for nine months, the right being more severely affected. For some months prior to her attendance at hospital, she had been employed in a restaurant kitchen operating a dish-washing machine. Part of her task was to remove the dishes from the machine and to place them in a drying rack. The latter, through a defect, required that the dishes be forced into position, and this she did by firm pressure with the base of the palm of the right hand. After a few months, she noticed pain in the palm of the hand, with numbness of the thumb and index finger, and commenced to do the same movement with the left hand ; symptoms followed in this hand shortly afterwards. Examination showed severe wasting of the thenar eminence on the right, and less severe wasting on the left. The abductor brevis and opponens pollicis on the right were paralysed, those on the left were weak. There were no trophic changes present, and there was only very slight impairment of perception of pin-prick over the terminal phalanges of the right thumb and index finger. At operation on April 13, 1948, the right transverse carpal ligament was divided. The median nerve was freed from rather firm adhesions in the carpal tunnel, the nerve sheath appeared thickened. The nerve was slightly enlarged at the proximal border of the ligament. The very slight sensory disturbance recovered rapidly, but on February 17, 1949, no motor recovery had taken place.

Comparing the two groups of patients, those presenting with unilateral and those presenting with bilateral palsies, three main points of difference are apparent ; these are concerned with age, sex and rate of onset, as will be seen from the table.

	Age					*Average duration of symptoms*
	Min.	*Max.*	*Aver.*	*Male*	*Fem.*	
Unilateral palsy	19	69	35	4	4	3 months*
Bilateral palsy	40	53	48	1	5	3½ years

*Excludes Case 5, as symptoms had been stationary for many years before advice was sought.

Unilateral palsy therefore tends to occur in relatively young subjects of either sex, whereas bilateral palsy is far more commonly seen in middle-aged women and has a very much more insidious onset. A mechanical source of trauma was described by all the 5 male patients concerned, and by 2 of the female patients (Cases 2 and 14). The remaining female patients were all engaged in the performance of heavy housework and laundry. It may therefore be concluded that median nerve palsy from compression at the wrist or palm is rare in young subjects in the absence of localized injury either by pressure of an external body or by deformity of the wrist or carpus, whereas the condition may arise in women as a result of apparently normal activity of the hands.

The clinical findings were similar in the two groups, although the disturbance of muscle function tended to be more severe where the condition was bilateral. Trophic disturbance was present in the majority of patients, and appeared to bear a definite relationship to the degree of loss of sensation. In all cases sensory recovery preceded motor, and was usually

very rapid, and in every case, with the exception of one (Case 14), the ultimate recovery of function was very satisfactory.

It remains to find an explanation of the mechanism of this type of median palsy, and in particular the mechanism of the condition when it affects both hands.

In the carpal tunnel, the median nerve lies in a relatively confined space, bounded posteriorly by the sheaths of the flexor tendons, and anteriorly by the transverse carpal ligament (flexor retinaculum). In spite of the confined space, the median nerve is freely mobile in a longitudinal direction to the tunnel, and observation on the cadaver by the writer has shown that this mobility persists both in flexion and extension of the wrist. Tension on the nerve can only be produced by simultaneous dorsiflexion of the wrist, extension of the elbow and abduction of the shoulder to more than a right-angle. This would suggest that tension on the nerve, in the absence of any deformity of the wrist, does not play any part in the production of median nerve lesions at this site.

Brain, Wright and Wilkinson in discussing the ætiology of the paralysis in their 6 patients consider that the palsy arises as a result of compression of the nerve in the carpal tunnel by repeated dorsiflexion of the wrist, that it has an ischæmic basis, and that its occurrence in middle-aged and elderly subjects indicates that vascular degeneration plays a part. In support of their theory they report the results of experiments with a tambour placed in the carpal tunnel, which demonstrated that the available space for the median nerve was much smaller in dorsiflexion of the wrist than in the mid-position. The same writers refer to the work of Denny-Brown and Brenner (1944*a*) in support of their statement that the paralysis is ischæmic in origin. It is significant, in this connexion, to note that Denny-Brown (1944*b*) refers to the relatively more severe loss of motor as opposed to sensory function after compression injury to peripheral nerves, and the rapid recovery of sensation that occurs. This was a very constant feature in the present series of patients.

Brain, Wright and Wilkinson also refer to the work of Denny-Brown and Brenner (1944*b*) in their explanation of their operative findings; the swelling and redness of the nerve at the upper border of the carpal tunnel indicating compression within the latter structure. This same swelling at the upper border of the carpal ligament was observed in all the cases of the present series, although this was not marked, and was not associated with any abnormal colour. Harris (1947) criticized the observations of Brain, Wright and Wilkinson, and suggested that the median nerve is normally enlarged and of pink colour above the carpal tunnel. Reference to the standard textbooks, however, reveals no reference to these features; Quain (1909) states "somewhat enlarged and of slightly reddish colour it here separates into two parts of nearly equal size . . .", i.e. at the *lower* border of the transverse carpal ligament. Piersol (1930) states that the median nerve spreads out into a reddish gangliform swelling at the lower margin of the carpal ligament. Gray's Anatomy (1930)

makes no reference to any enlargement or coloration of the nerve. Personal observation of the median nerve in the cadaver showed that the calibre of the nerve is the same at the proximal border of the carpal tunnel as in the tunnel itself, the only change being a very slight flattening within the tunnel. It seems clear beyond doubt, therefore, that enlargement of the nerve in this situation is abnormal, and can be attributed to compression within the tunnel.

Heavy manual work undertaken by middle-aged and elderly women must be of common occurrence at the present time, and is likely to involve repeated extension of the wrist or wrists. If this is so, the syndrome of median nerve compression in the carpal tunnel might be expected to be rather common, whereas it is in fact not frequently encountered. It would seem necessary to postulate some factor in addition to repeated wrist extension in the production of this condition. The added factor could be either an external or an internal compression of the nerve. The external factor is clearly often present in the form of a scrubbing brush, saucepan handle or lawn-mower ; an internal factor is not at once apparent. Further observations on the cadaver have led the writer to the conclusion that mere passive extension of the wrist with or without external compression of the palm is insufficient to account for median palsy, and that the explanation lies in more dynamic factors operating in the palm.

Examination of the carpal tunnel confirmed that the available space was lessened with the wrist in extension, but that in this position the median nerve remained freely mobile. The effect of exerting tension on the flexor muscles was therefore investigated, and it was found that tension on the flexor tendons with the fingers held, and with the wrists lightly dorsiflexed, resulted in the median nerve becoming subject to considerable friction and resistant to slight tension. During this manœuvre it was not possible to insert the tip of the little finger into the carpal tunnel. This observation was confirmed on five separate occasions. When one considers this process occurring during life another factor tending to compress the carpal tunnel is present. The palmaris longus tendon is attached to the distal half of the transverse carpal ligament prior to its attachment to the palmar fascia, so that with the wrist in any degree of dorsiflexion, flexion of the fingers against resistance will result in compression of the median nerve between the flexor tendons posteriorly, and the palmaris longus anteriorly. Thus a state of affairs arises strictly comparable to that which obtains in the production of a friction neuritis of the ulnar nerve in cubitus valgus, and with or without the presence of a hard object compressing the palm it is suggested that compression by muscle action is the principal factor in the production of the syndrome of the carpal tunnel.

Conclusions

Median nerve palsy may arise on one or both sides during the course of a normal occupation, without obvious evidence of direct trauma. In younger subjects, it is usually associated with pressure on the palm

of the hand by some hard object used over a relatively long period, and affects the sexes equally. Women are more often affected in middle age, and in this group direct pressure plays a less obvious part. It is suggested that in both young and old subjects muscular contraction is the primary cause of paralysis, and that external pressure or bony injury may be contributory.

In those cases where motor symptoms and muscle wasting are not pronounced, rest seems to be adequate treatment, and 6 of the 8 patients with unilateral palsy made a complete recovery in this way. It is, of course, apparent that symptoms may return on resuming full use of the hand, but so far none of the patients has noted any renewal of symptoms. Two men were fitted with protective pads to the palm of the hand and have returned to their occupations without relapse. In all cases where motor symptoms are severe conservative treatment is unlikely to be of benefit, and surgical division of the transverse carpal ligament is indicated. This applied to all the patients with bilateral symptoms. So far the writer has not had the opportunity of treating an early case of this sort by conservative measures.

The effect of operation may be compared with the procedure of neurolysis undertaken to free involved peripheral nerves from scar tissue. It is not uncommon to find that the progress of recovery of a nerve lesion in continuity is arrested, and that following neurolysis rapid improvement occurs in spite of the finding of a nerve of macroscopically normal appearance, and only minimal scar tissue. It must be assumed in these cases that the blood supply of the nerve is disturbed, and that operation restores this to normal. The fact that the median nerve showed only slight abnormality in those patients of the present series subjected to operation suggests that the improvement that followed was due to the same factors.

Summary

Fourteen patients with median nerve palsy are described ; in 8 the condition was unilateral, and in 6 it was bilateral. 6 of the 8 unilateral palsies were mild and responded well to immobilization of the wrist and protection of the palm. All of the 8 bilateral palsies were severe and were treated surgically by division of the transverse carpal ligament. The result was good on 7 occasions. The ætiology of the condition is discussed, and it is concluded that compression of the median nerve between the flexor tendons posteriorly, and the carpal ligament and palmaris longus anteriorly is a factor in its production, and is a major factor when the condition occurs in both hands in middle-aged subjects. Attention is drawn to the close association of sensory and trophic changes, and the rapidity with which these phenomena respond to treatment.

The writer is indebted to the following for permission to record their operative findings : Mr. G. N. Golden, Mr. H. A. C. Chalmers, Mr. St. J. D. Buxton, Mr. E. N. Brockway and Mr. G. C. Jennings.

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LEGENDS FOR PLATE I

FIG. 1. (Case 5).—Volar aspect of hand showing severe wasting of the abductor pollicis brevis muscle, and a trophic ulcer on the index finger.

FIG. 2 (Case 5).—Dorsal aspect of hand to show trophic change in the nails and atrophy of the terminal pulp of the ring finger.

FIG. 3 (Case 10).—Volar aspect of right hand showing atrophy of the thenar eminence, dry shiny skin over the thumb and index fingers, and atrophy of the terminal pulp of the thumb and index finger.

FIG. 4 (Case 10).—Lateral aspect of hand showing the complete wasting of abductor pollicis brevis.

To il

PLATE I

Plate I

FIG. 1.

FIG. 2.

FIG. 3.

FIG. 4.

To illustrate article by David Kendall.

THE HUMAN PYRAMIDAL TRACT. XVIII
AN ANALYSIS OF ITS PATHOPHYSIOLOGICAL STATUS

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THE general concept of pyramidal physiology in man was formulated early from results obtained through research on the effect of diseased processes upon the tract and those of a few select subhuman animal experiments. By far, the majority of pathological observations on the pyramidal tract was made before 1900 and the pertinent ones were contributed by men both distinguished and influential in the neurological world. However, the question can be raised as to whether the biggest gap in our overall knowledge of this motor fasciculus is not due to lack of scientific studies in the pathological field. Although a century has elapsed since the first important study on the pyramidal tract was made by Türck (1851–1853), no overall correlation or evaluation has been made, as far as I have been able to ascertain, between specific quantitative degeneration in the bundle which may have been caused by lesions and the degree of voluntary motor deficit. Since organic disease in the central nervous system is said to depend upon degeneration of nerve fibres, since the pyramidal tract may have a much more complex make-up than previously thought and since it is an important characteristic of the scientific method to strive toward quantitative interpretations, it was felt that a study directed toward this end on the bundle might be of fundamental value.

MATERIAL AND METHODS

The background for the material presented was obtained by three methods of approach as follows: Examination of the research articles published by the early investigators who were almost entirely responsible for our concept of pyramidal physiology. This was done with emphasis being placed on their pathological observations. Secondly, a pathological analysis of 11,947 cases found in the modern literature in hundreds of different medical volumes, in each of which the patient showed some degree of motor paralysis. Lastly, personal observations made on the degenerated state of axons located in the pyramids of 236 medulla oblongatas which were removed from individuals who had suffered from voluntary motor paralysis (Lassek, 1944, 1945, 1946).

Although it has taken more than a decade to accumulate the data presented in the article, it may be possible that some findings pertinent

to the problem have been missed. It is felt, however, that the results may represent rather accurately the status of pyramidal physiology based on pathological considerations in man up to date.

Results

It is believed that the men who were most influential in developing our first concepts of cerebral localization in man and the view that voluntary motor function is confined to the pyramidal tract were the following: Türck (1851–1853); Bouchard (1869); Charcot (1883); Ferrier (1879, 1890); and Hughlings Jackson (Taylor, 1931). These investigators did not all use the same approach. Türck, Bouchard and Charcot, probably the most important of the five from the standpoint of this article, directed their efforts largely to correlating secondary degeneration in the pyramidal tract and the symptomatology from human paralytic individuals. Ferrier did pioneering research on the electrical stimulation of the cerebral cortex in the monkey but also selected pathological cases from the literature in an attempt to prove his views. Hughlings Jackson was a brilliant theorist who specialized in epilepsy but apparently made some pathological observations on secondary degeneration. Türck published several articles whereas Charcot, Ferrier and Jackson wrote prolifically concerning their views. Bouchard contributed a single pioneering monograph on his personal discoveries. I have also examined the original papers, reviews, monographs and texts of many other early writers on this field but feel that basically their results and opinions only harmonize with the views of the five investigators mentioned above.

In analysing the findings of the pioneers, Türck (1851–1853) can be considered first. Although not the earliest to focus attention on the pyramidal tract as a possible conductor of voluntary motor impulses, Türck was the discoverer of secondary degeneration in the central nervous system via the pyramidal tract. He published his results about a year after Waller's original contribution on the peripheral nervous system. His first report was based on a study of a few hemiplegics with cerebral pathology. He found that lesions of the internal capsule caused secondary degeneration which he traced down through the brain-stem and spinal cord. By contrast, he claimed that lesions limited to the lenticular and caudate nuclei or optic thalamus did not. In this and a later publication, no actual correlative or quantitative data was given in regard to loss of pyramidal fibres as far as I have been able to ascertain.

Bouchard (1869) studied secondary degeneration in the pyramidal tract in the spinal cord in 32 old hemiplegics who had a duration of symptoms averaging forty-six months. He was the first to use hardening and staining (carmine) and one of the few to correlate destruction of pyramidal fibres with the symptomatology. He stated that there are some pathological conditions which cause paralysis without producing secondary degeneration in the pyramidal tract and that some normal nerve fibres

may remain in the degenerated field ; these undestroyed nerve fibres he believed were either respected by the injury or they arose from other parts. Outside of this, he gave no quantitative data on the degree of degeneration in the pyramidal tracts he observed. The contractures of the muscles he felt were due to scar formation (sclerosis) in the tract. The strength in the muscles he found to be quite variable in hemiplegics ranging from very feeble, feeble, strong, quite strong, and very strong.

Charcot (1883) claimed to have spent fifteen years during which he correlated the extent and nature of cerebral lesions, descending secondary degeneration and motor paralysis. He intimated that he examined as many as 200 cases in this respect during this interval. From the quantitative viewpoint, his analysis seems to be general and quantitatively nonspecific. He felt certain that not all the types of cerebral lesions which cause paralysis are accompanied by degeneration in the pyramidal tract. For example, he stated that the majority of tumours only displace and separate nerve fibres without destroying. He was also apparently much influenced by the investigations of Ferrier on the monkey and he correlated his studies on man with the Englishman's extirpation results. In harmony with Ferrier's view, he localized the probable origin of the pyramidal tract to the anterior and posterior central gyri of the cerebral cortex.

Ferrier (1879, 1890), another early champion of cerebral localization, apparently made no direct pathological contributions of his own on the pyramidal tract. In his 1879 article, he cited 34 cases selected from the literature in 8 of which actual degeneration was observed ; in none, however, was there any quantitative estimate of the possible degree. Later (1890), he made passing reference to 483 cases of localized lesions of the cerebral cortex collected by a Dr. Ewens which had caused paralysis of the opposite side of the body but he mentioned nothing as to the possible involvement of the motor bundle. I gain the impression that he was considerably influenced by the results of his own ablative experiments on the cerebral cortex of the monkey, more so than from any personal analysis of suitable human material.

In reading over the collected writings of Hughlings Jackson (Taylor, 1931), the eminent English neurologist, who specialized mostly on the disease entity, epilepsy, I have been able to find but a few references to any pathological observations made by him. He did state that paralysis depends upon destruction of fibres but thought that destruction was scarcely a correct word. By it, he did not necessarily mean that the nerve fibres are broken up but simply that there is a change in them that destroys their function. For instance, he cites the example that in epileptic hemiplegia the axis cylinders only temporarily lose their function due to the excessive quantity of force they have had to carry. It was his opinion that tumours act very indirectly and that in these destruction of the pyramidal tract is at most very slowly effected. A small quantity of the motor tract, he thought, could be lost without producing obvious

motor symptoms and this could be proved at post mortem. To him, there were all degrees of paralysis and all degrees of recovery.

It seems that, without exception, the early investigators and writers before the turn of the century were uniform in their belief that paralysis could be caused by indirect as well as direct effects on the pyramidal tract and particularly in the cases of space-consuming masses such as tumours and abscesses or meningeal involvement and superficial lesions of the cortex. It was also agreed by everyone that the motor cortex was more widespread than area 4 and I believe that Ferrier's investigations on the monkey were largely instrumental in developing this view.

The next important development in our overall concept of the pyramidal tract developed in the early 1900's, namely the narrowing of its zone of origin in the cerebral cortex. Here again animal experimentation seems to have led the way. Grünbaum and Sherrington (1901–1902) with their electrical stimulative experiments on subhuman primates, localized what is now called the true motor cortex to area 4. Campbell (1905), studying the normal structure of the Betz cells in man and Holmes and May (1909), using the method of retrograde degeneration in man and other animals, were also partly responsible for crystallizing the idea that the pyramidal tract arose solely from area 4. These findings, however, did not in any way modify the existing view that the pyramidal tract was the great voluntary motor path in man.

In reviewing the literature since 1900, I was able to locate but few quantitative investigations limited solely to pyramidal tract studies in man. Peculiarly, most of these are concerned with reports on clinical cases of profound motor paralysis without noticeable destruction being observed in the pyramidal tract at autopsy (Bielschowsky, 1916–1918; Finkelnburg, 1913; Hoestermann, 1912; Rhein, 1913; Spielmeyer, 1906). Because of this, together with the vague pathological reports found among the early investigators, I felt it would be of value to study what scattered case reports in the literature I might locate which show voluntary motor paralysis. This was done with the hope that some would give valuable pathological data regarding the pyramidal tract. With this approach, over 12,000 paralytic cases caused from the various pathological entities have been examined. 1,743 of these were autopsied and of these observations were made on the status of degeneration in the pyramidal tract in 437 (Table I). Of the 437, 236 represent the author's personal published cases (Lassek, 1944, 1945, 1946). In most of all these, the lesions were in the cerebral hemisphere.

Probably the most ideal specimens to study in determining the functional role of the pyramidal tract would be those in which the bundle alone is involved. No unequivocal cases in this respect have been found. Table II shows the number and status of destruction as reported in each of the pathological entities. Complete degeneration was found described in 26 cases, severe in 59, slight in 58, a normal tract was observed in 188 paralytic individuals (mostly tumours) and finally in 106 non-quantitative

TABLE I.—SHOWING THE NUMBERS OF INDIVIDUAL, GENERAL AND TOTAL PARALYTIC CASES, TOGETHER WITH AUTOPSIES PERFORMED AND PYRAMIDAL TRACTS EXAMINED PATHOLOGICALLY, ALL OF WHICH WERE FOUND FROM AN EXTENSIVE SEARCH IN THE LITERATURE*

Pathological entity	*Individual cases*	*General cases*	*Total cases*	*Autopsies performed*	*No. cases with observations on pyramidal tract*
Inflammations ..	1,232	806	2,038	307	32
Tumours	1,092	242	1,334	643	139
Vascular	726	526	1,252	396	148
Trauma	631	412	1,043	126	12
Toxins	100	244	344	22	2
Scleroses	592	63	655	145	60
Congenital	79	285	364	18	17
Unclassified	384	4,769	5,153	86	27
Totals	4,836	7,347	12,183	1,743	437

*The cases listed under " general " were selected from articles where the authors reported statistical findings on a series of patients. By contrast the " individual " cases were those which gave the history, physical examination and diagnosis and sometimes the pathology for each patient.

TABLE II.—GIVES AN INDICATION OF THE STATUS OF DEGENERATION IN 437 HUMAN PARALYTIC CASES CAUSED BY THE VARIOUS PATHOLOGICAL ENTITIES AND WHERE THE PYRAMIDAL TRACT WAS OBSERVED AT AUTOPSY

Status of degeneration	*Vascular*	*Tumour*	*Scleroses*	*Inflammation*	*Unclassified*	*Congenital*	*Trauma*	*Toxin*	*Total*
Complete ..	9	10	4	1	0	1	1	0	26
Severe ..	22	12	9	2	6	2	5	1	59
Slight.. ..	22	7	15	7	5	0	1	1	58
Normal tract	67	102	2	1	2	12	2	0	188
Non-quantitative	28	8	30	21	14	2	3	0	106
Totals	148	139	60	32	27	17	12	2	437

descriptive terms were employed. In the last, it was merely stated that degeneration was present without mentioning the degree. This leaves 331 in the series actually giving quantitative data.

If we accept the view that the development of abnormal motor function in man depends primarily upon degeneration of pyramidal tract fibres, then an analysis of the 331 cases giving quantitative information presents a somewhat contradictory picture. I have not been able to find any distinct correlation, whatsoever, between the degree of destruction in the motor bundle and paralysis. First, it is possible to have what is judged by clinicians to be a chronic complete hemiplegia or severe paralysis with the pyramidal tract in one of the following conditions : with total, severe, moderate or slight loss of fibres or with its neurons in what is

judged to be a normal morphological state. Secondly, it is also possible to have involvement of the central nervous system (the pyramidal tract ?) by lesions so that the syndromes vary from simple to more complex deficits. For example, pathologic reflexes such as the Babinski sign may be the only evidence of disturbance present, or altered tendon reflexes alone, or only interference with tone, or any possible degree of paralysis or finally any combination of these.

Discussion

To function normally, the descending bundle called the pyramidal tract must have a large number of afferent neurons connecting with its cells of origin (the Betz and possibly others). Where these come from and exactly how they act is not understood but they probably are concerned to some extent with initiating and maintaining the motor impulses. If the pyramidal tract in itself is the great motor bundle in man, then it would seem that the pyramidal circuit, whatever it may be, could be functionally affected by pathological lesions which either destroy or inhibit. The results of the present study indicate that paralysis of an enduring nature can occur in a great many individuals without evidence of degeneration in the pyramidal tract. The majority of paralytic cases (57·5 per cent) in the collected series shows normal pyramidal tracts. This may mean that inhibition plays a significant role. Whether such arrest can result from direct or indirect pressure effects from the lesion or both, I am not in a position to say. That the afferent impulses to the cells of origin of the pyramidal tract may be adversely affected by cerebral lesions in man is indicated by the interpretations of a number of investigators (Bielschowsky, 1916–1918; Finkelnburg, 1913; Hoestermann, 1912; Rhein, 1913; Spielmeyer, 1906). Another form of inhibition of motor impulses may be that which occurs following certain cases of convulsions which Jackson (Taylor, 1931) designated as epileptic hemiplegia. He explained this as being due to exhaustion from the excessive quantity of force the fibres had to carry. Still another possibility to consider is the exact role of the extrapyramidal pathways which reach the cord by means of two or more neuronal connexions. Whatever the true status of pyramidal function may be, I feel that progress in our understanding of it in man will develop largely through scientific investigations where the quantitative effects of lesions, pathological or surgical, on the pyramidal neurons will be studied.

The type of pathological lesion and its chronicity are of importance as to whether degeneration in the pyramidal tract occurs or not. The evidence indicates that cerebral tumours in the majority of instances do not cause secondary degeneration in the motor bundle although paralytic symptoms may be chronically present. This harmonizes with the view of all the early and some recent investigators in the field. Some cerebrovascular injuries may also fall into this category although in general they are more destructive to pyramidal neurons than the tumours (Lassek,

1945). The effect of the other pathological entities has been little investigated but there is some indication that in certain congenital cases where there are malformations in cerebral development the pyramidal tract may be morphologically intact although pronounced paralysis may be present (Lassek, 1946).

One of the criticisms which can be levelled against an analysis of this nature is that a great many individuals were involved in the scattered clinical and pathological interpretations. I have noticed that the criterion of motor deficit in voluntary muscles varies according to the standards of the observer. One may judge it in terms of " power " in the muscles, another in terms of " movement " and still another in terms of " gait." It is realized that the ideal approach in attempting to determine the true status of the pyramidal tract in man would be for one or more careful scientific observers to have access to a large series of paralytic patients caused by the different types of lesions who could study them both clinically and pathologically. However, the purpose of the present study has been merely an attempt to determine what correlation can be made between the pathology and function of the pyramidal tract in man on the basis of what has been reported during the past one hundred years.

It seems to me that, in the final analysis, the findings here reported lead to perplexing questions regarding the function of the human pyramidal tract. It is impossible to judge accurately what its role may be. It leaves open the questions as to how all the pathological entities may affect the pyramidal neurons, what is the role of inhibition by lesions on its descending fibres, how the afferent fibres connecting with its cells of origin may react to cerebral pathology and finally what is the exact role of the extrapyramidal pathways in man ?

It is probably superfluous to say that the mechanism in the human nervous system which controls the movements of voluntary muscles may be very complex and that to solve the question constitutes a challenge to investigators interested in the subject. Walshe (1947), in his recent analysis of the role of the pyramidal tract in willed movements, regards it as a path made up of internuncial neurons which are activated and moulded by controlling cortical afferent patterns of excitation. In itself, it initiates and directs nothing but derives its motive and directive power from outside sources. The easiest approach to the problem may be first through co-operative research on the pyramidal tract to determine its physiological role since we have more known facts regarding its constitution than the extrapyramidal pathways. An important anatomical characteristic of this fasciculus is its isolation in the pyramids of the medulla where the effects of pathological lesions above can be easily observed. As the overall situation now stands, it seems to me that the results of some of the more accurately controlled animal experiments on the subhuman primates may have much more scientific and practical value than the collective pathological investigations on man, at least those which have been reported up to date.

Conclusions

(1) There is little evidence that the phenomenon of secondary degeneration in the human pyramidal tract has been extensively studied from the scientific or quantitative viewpoint during the past century.

(2) Motor paralysis of a chronic nature apparently can occur in man with the pyramidal tract in one of the following conditions: with total, severe, moderate or slight loss of fibres or with its neurons judged to be in a normal morphological state.

(3) Every gradation of motor deficit or alterations of reflexes can occur from pathological involvement of the central nervous system.

(4) It is difficult or impossible to judge what the true function of the human pyramidal tract may be on the basis of the pathological data available.

(5) If the pyramidal tract plays a major role in voluntary motor function, then it must be assumed that either the activity of its neurons can be inhibited indirectly in many instances by cerebral lesions or that afferent fibres playing upon its cells of origin may be affected.

(6) The type of pathological lesion is important as to its destructive effect on the pyramidal tract.

(7) It may be that the extirpation results of animal experimentation upon subhuman primates have more scientific value than the collective pathological investigations on man.

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SURVIVAL IN DISSEMINATED SCLEROSIS : A CLINICAL STUDY OF A SERIES OF CASES FIRST SEEN TWENTY YEARS AGO

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THE literature of Disseminated Sclerosis contains relatively few contributions devoted to description of the clinical course of the disease. The average duration of life from the onset of the first symptoms until death has usually been estimated from study of old hospital records. This entails some artificial selection of material for only severe cases are admitted to hospital. Further, in deciding the date of onset, everything depends on the patient's ability to recall early symptoms. If they already are in a fairly advanced state, as many are when first seen in hospital, they will probably be unable to do so. The care taken in eliciting this information is another factor which must influence results. Even when these difficulties can be overcome by personal investigation there still remains the difficulty of deciding whether some early symptom bears any relation to the disease or not. One has only to study the journal of the unfortunate Barbellion (1919) or the Diary of Augustus d'Esté (1948) to appreciate this point, and as McAlpine (1946) suggests, the onset of the disease and the first appearance of symptoms may not coincide ; there may be a latent asymptomatic period as in rabies and in syphilis of the nervous system.

Charcot, while admitting the gravity of the prognosis, recognized the occurrence of remissions and their favourable effect. Pierre Marie supported him in the belief that the disease might be arrested at any stage in its course. Gowers thought the duration lay between three and six years and this may be compared with Bramwell's (1905) experience of about seven years. Later in 1917 Bramwell reviewed a larger series and found that of those that had died (106 cases) only 10 had lived longer than 21 years. The report of the American Association for Research in Nervous and Mental Diseases (1921) has little to say about the natural course of the disease but mentions that the common causes of death, unless there be bulbar involvement, are tuberculosis, ascending infections of the kidneys, sepsis from decubitus and pneumonia. In the past quarter of a century—probably through the tendency to recognize the disease in its more early stages—a more encouraging prognosis has been given. Thus, in a small series of fatal cases Brain (1936) found the average duration from onset to death was 12·5 years. Among his living cases at that time it was 13·6 years. Later he notes (1947) that survival for

twenty years is not very rare and that one of his patients was alive after twenty-nine years. This experience is similar to that reported from Germany by Drobnes (1937), Vierheilig (1940), each of whom followed up a large series of hospital cases. The average duration of the disease in the former's cases was 12·5 years and his record twenty-seven years. More recently statistical surveys of large series of hospital cases have been published by Sällström (1942), Thygesen (1947), Müller (1949). Thygesen found that about a quarter of the patients he examined after eight to fifteen years were wholly or partially free of symptoms and able to work. Müller calculated that the average duration of the disease probably lies between sixteen and thirty-four years.

Other authors have related their experience in relation to prognosing on the character of the early symptoms. Thus, Brain believes that acute extensive signs in young adults have a poor prognosis, the chronic spinal form of middle age a better and the remitting type the best prognosis. Birley and Dudgeon (1921) observed that patients in whom the initial disturbance was relatively sudden may remain in perfect health for months or years at a time. They were of the opinion that more cases than has commonly been supposed recover from the initial symptoms and remain well permanently. Foster Coates (1930) pointed out that when the initial symptoms made their appearance insidiously they were unlikely to remit as fully as when they appeared relatively suddenly. Brown and Putman (1939) found that symptoms suggestive of a minimal lesion such as central scotoma, diplopia and subjective sensory disturbances confined to one extremity, tend in the natural course to regress and to leave little after-effects. In contrast more severe or more disabling symptoms due to larger or scattered lesions such as paraplegia, ataxia and mental deterioration regress imperfectly and usually leave behind some permanent impairment of function. They found too that the natural tendency of all symptoms to regress becomes less as time passes and relapse follows relapse. The McIntyres (1943) who analysed the course of the disease in a series of cases commented on the long periods of survival in many instances which were greater than their previous experience had led them to suppose. Most authorities recognize the three main clinical forms of the disease : the acute progressive, the relapsing and remitting, and the chronic progressive type. The tendency is also not to separate acute neuromyelitis optica and acute disseminated encephalomyelitis from disseminated sclerosis but to regard these forms as being closely allied or related to a common pathological process which has protein clinical manifestations.

The purpose of this paper is to review a group of cases which was first seen twenty years ago. The number is small (40 cases) and conclusions are tentative. It had been suggested that disseminated sclerosis might be more common in rural than in urban districts, Morawitz (1904), Steiner (1922), Adams and others (1924), and it was decided to investigate the actual incidence of the disease in a rural area, namely North Wales

(Allison, 1931). Altogether 126 cases were reported but only 65 of these were found to have disseminated sclerosis and there were only 40 who were alive at the time and had their homes in the area. In these 40 cases the date and mode of onset of the disease were ascertained so as to correlate the information with the places where the patients were living at the time. No support was found for the supposed rural distribution but the data relating to the dates and modes of onset is of some value as the subsequent fate of these patients is now known.

A review of the original clinical features presented will first be given, then the duration of the disease will be discussed and the state of the survivors considered.

Original Clinical Material

Table I (inset) gives a synopsis of the previous history, the age and mode of onset, duration of the disease and principal clinical features when the patients were first seen. There was a preponderance of females, 25 women and 15 men. This feature is often seen in small series (Brain, 1930), though some observers such as Müller (1949) believe that the sex distribution among the population affords no explanation as to the surplus in women.

Age of onset.—The difficulty often encountered in deciding this point is illustrated in Cases 1 and 2 (*see* Table I). Though in the former it was thought probable that the onset was in 1917, it could have been much earlier, in 1895. In Case 2 diplopia was observed at the age of 15 but, as it lasted so short a time and was related to injury, it was considered more probable that the first definite signs of the disease appeared in 1925 when the patient was aged 20. These points are mentioned to indicate that, though every effort was made to elucidate early possible symptoms, discrimination was exercised in not stretching this limit too far.

Table II.—Age of Onset Expressed in Decades

Age	0–10	11–20	21–30	31–40	41–50
No. of cases	—	5	21	10	3

The above table gives the age of onset in 39 cases for in one instance the information was unreliable and it has not been included. The youngest age of onset was 13 years (Case 37), the oldest was 50 (Case 7). In half the number the onset was in the third decade. There were 13 patients or about one-third in whom the first symptoms occurred after the third decade. This is about the same proportion as occurred in the larger series of Friedman and Davison (1945) who were interested specially in the symptomatology and course of the disease in middle-aged and older persons.

Mode of onset.—In no case was the onset associated with fever, meningeal signs and clouding of consciousness. Not infrequently there was an antecedent history of "influenza" but feverishness had subsided and

the patients were convalescent before symptoms were noticed. The individual modes of onset in all the cases are set out in column 3 of Table I. In half the number the disease began with a single symptom or, as Brown and Putman (1939) postulate, with symptoms the character of which suggested that the lesion responsible was minimal in its extent, e.g. acute retrobulbar neuritis or diplopia with facial palsy. In the other half symptoms appeared which suggested a more extensive lesion, e.g. paraplegia, or there were symptoms pointing to the occurrence of active lesions at different sites in the nervous system, e.g. emotional disturbances simulating hysteria, with ataxia. The different modes of onset based on this arrangement are summarized in the table given below.

TABLE III.—MODE OF ONSET

With symptoms suggesting a minimal lesion :

	Cases
Weakness of one leg	9
Acute retrobulbar neuritis	7
Subjective sensory disturbance	2
Diplopia and facial palsy	1
Diplopia	1
	20

With symptoms indicating more extensive or multiple lesions :

	Cases
Paraplegia	5
Ataxia with weakness of legs	4
Weakness of one leg with sensory disturbance	3
Hemiplegia	2
Hemi-anæsthesia with monoplegia	2
Paraplegia with weakness of one arm	1
Root pains, intent. tremor, dysarthria	1
Ataxia and emot. hysterical symptoms	1
Weakness of one leg with sens. disturbance and diplopia	1
	20

Occurrence of initial remissions.—It is noted in Table I, column 4, whether the initial symptoms remitted completely, partially (improving but leaving some residual disability) or did not improve, slow progression of the malady resulting. In this series a complete or partial remission followed the onset in 32 cases or 80 per cent of the total. There were 17 complete and 15 partial initial remissions. The remaining 8 cases in which the symptoms did not remit and the disease slowly progressed all had a long history when they were first seen. It is possible, therefore, that earlier transitory symptoms may have occurred but that the patients were unable to recall them.

In Table IV the natural tendency to initial complete or partial remission is contrasted with the different modes of onset. It will be seen that complete remissions followed an onset by acute retrobulbar neuritis, subjective sensory disturbance or diplopia in all the cases so affected. In contrast,

TABLE IV.—RELATIONSHIP BETWEEN MODE OF ONSET AND TENDENCY TO NATURAL REMISSION

Initial remission	*Mode of onset*	*Cases*
Complete (17 cases)	Acute retrobulbar neuritis	7
	Subjective sensory disturbance	2
	Weakness of one leg	2
	Diplopia and facial palsy	1
	Diplopia	1
		13
	Symptoms suggesting more extensive lesions :	
	Paraplegia	1
	Root pains, intent. tremor, dysarthria	1
	Ataxia and hysterical symptoms	1
	Weakness one leg with sens. disturbance	1
		4
Partial (15 cases)	Paraplegia	3
	Ataxia with weakness of legs	3
	Weakness of one leg with sensory disturbance	2
	Hemiplegia	1
	Weakness of one leg, sensory disturbance and diplopia	1
	Paraplegia and weakness of one arm	1
	Hemi-anæsthesia with monoplegia	1
		12
	Symptoms suggesting a minimal lesion :	
	Weakness of one leg	3
		3

a complete remission was unusual after a motor type of onset—weakness of one leg, paraplegia or ataxia. Brown and Putman's conclusions are supported for in only 4 out of the 17 cases that remitted completely did the initial symptoms suggest that there were extensive or scattered lesions, whereas in the partially remitting cases there was a preponderance of such symptoms.

One might proceed further and contrast the different modes of onset and the lengths of the initial remissions with the subsequent course of the disease, especially in relation to expectancy of life. But this cannot be done at present because 12 of the cases are still alive and the duration of their illnesses is not yet known. It should be noted, however, that although there was a high proportion of cases in this series showing an initial remission, the length of this was usually short being under eight years in all but three instances—Cases 4 (over twenty-seven years), 40 (over twenty-four years) and 35 (ten years).

A feature observed in the remitting and relapsing cases was that in several the same symptoms as were present at the onset recurred in the first relapse. This will be referred to later. Motor symptoms rarely recov-

ered after the first relapse but the same tendency to complete recovery as was seen at the onset characterized acute retrobulbar neuritis and subjective sensory disturbances when these appeared subsequently in the course of the disease.

Length of history and clinical state when first seen.—These are considered in columns 5 and 6 of Table I. The average length of the histories in 1929 for the 40 cases was about ten years. Only the abnormal findings are noted in the columns summarizing the clinical state. "Slight disability" means that it was not such as to interfere materially with the patients' working capacity, " Moderate disability " that the patient could undertake light work but that his working capacity was impaired. " Severe disability " means that the patient could walk or stand only with assistance or that he was confined to bed. In 1929 there were 7 patients with no disability or slight disability only, 14 with moderate disability, and 19 who were severely disabled.

Duration of the Disease

Enquiries were set on foot this year with the object of finding how many of the patients originally seen had died and how many had survived. Though some difficulties were met all the cases were successfully traced ; 28 or 70 per cent had died, 12 or 30 per cent were still alive.

Copies of the death certificates were obtained in all but one of the deceased (Case 33) in which, however, there is evidence, based on the statements of the doctor and of relatives, that death occurred in 1940. The duration of the disease was estimated by subtracting the date of onset of the first symptoms from the year of death. The longest was thirty-four years. About 40 per cent lived twenty years or more. The shortest was eight years ; the average for the 28 cases was 19·5 years.

The 12 survivors were revisited and examined. The longest duration of the disease amongst these was thirty-nine years and 5 or nearly half had had the complaint for over thirty years, the average being 27·8 years.

The duration of the disease in the series as a whole may not be given at present owing to the high proportion of survivors. Obviously, however, when the fate of the latter is known, the average cannot be less than *twenty-two years* for this figure is about the mean of the two averages already given.

Table V.—Estimated Duration of the Disease (1949) in 40 Cases

Duration in years	*Deceased* (28)	*Survivors* (12)
15 or less	10	—
16–20	8	1
21–25	4	5
26–30	3	1
31–35	3	3
36–40	—	2

The duration of the disease in this particular series appears to be considerably above the figures usually quoted. But, as has been already stated, the latter are based for the most part on hospital material. I have not been able to discover any other follow-up similar to this where the course of the disease in a number of patients all living in the same district has been studied. These North Wales cases may have been more fortunate than the general run but, if so, this cannot be attributed to any special treatment. It is admitted that average durations of a disease of this type mean very little statistically unless studied side by side with ages of onset. Especial care was taken to determine the earliest symptoms and this would naturally tend to increase the duration of the disease in the series as a whole. Further, the preponderance of females may have had some influence for as Müller (1949) has shown the prognosis for cranial nerve, motor and sensory disturbances is somewhat better among women than men. But allowing for these possible factors it would appear that in a great number of cases the disease may run a longer course than is generally supposed. In the past the tendency possibly has been to regard survival for twenty to twenty-five years as exceptional. On the basis of this experience I would say that not until twenty-five years have elapsed from the first symptoms is one justified in assuming that either the disease is particularly benign in type or that the patient is resistant to its progression.

Period of incapacity in relation to the whole illness.—In a disease which may occupy so large a part of a patient's life it is important to try and assess how long he may be totally incapacitated and in need of adequate assistance. The duration of the period of total incapacity in those patients who were not incapacitated in 1929 and who died before 1949 is not known. The best available estimate, therefore, of the length of incapacity is obtained from the subsequent histories of those who were incapacitated in 1929. As Table I shows there were 19 such cases. The proportion of the total illness spent in this way by these patients is given in Table VI. Of interest especially are Cases 1 and 21 who are still alive after more than twenty years in the bedridden state. Having recently seen and examined them I find it difficult to believe that the absence of any serious decline is to any appreciable extent dependent on the nursing care they have received. Both patients have spent the entire period in their homes, confined to bed with the exception of brief excursions out of doors in wheeled chairs when the weather permitted. Case 18, now dead, is also noteworthy insomuch as she was bedridden for twenty-four years.

When the total duration of the illness is compared with the length of the state of severe incapacity it will be seen that about half the total period was spent in this state. The average duration of severe incapacity in the 17 patients who have died was at least ten years. Some patients such as Cases 1, 18, 21, 22, 32 were severely incapacitated relatively early in the course of their illnesses. In cases 26, 27, 35, the period of severe incapacity was relatively short.

TABLE VI.—DURATION OF TOTAL INCAPACITY AND TOTAL ILLNESS (19 CASES)

Case No.	*Onset of severe incapacity*	*Fate*	*Duration of severe incapacity*	*Total duration of illness*
1	1929	Survivor	20 years	32 years
3	1927	d. 1935	8 years	14 years
5	1919	d. 1929	10 years	18 years
6	1927	d. 1932	5 years	12 years
8	1927	d. 1936	9 years	18 years
9	1926	d. 1936	10 years	19 years
15	1919	d. 1930	11 years	21 years
18	1924	d. 1948	24 years	33 years
20	1922	d. 1936	14 years	29 years
21	1929	Survivor	20 years	33 years
22	1926	d. 1936	10 years	13 years
23	1924	d. 1929	5 years	10 years
25	1920	d. 1932	12 years	23 years
26	1928	d. 1934	6 years	22 years
27	1929	d. 1933	4 years	16 years
32	1923	d. 1933	10 years	14 years
33	1924	d. 1940(?)	16 years	34 years
35	1929	d. 1938	9 years	34 years
39	1927	d. 1936	9 years	21 years

Cause of death.—Post-mortem examinations were not made in any of the 28 instances in which death occurred. This is a circumstance upon which it is curious to reflect when it is considered how little is known of the pathogenesis of the disease. But the patients were living in outlying districts and presumably no diagnostic issue was raised. Disseminated sclerosis, *per se*, accounted for death in a number of cases in which the patient became progressively more helpless, demented, incontinent and finally relapsed into a coma which terminated in death. This coma might intervene suddenly and how unexpectedly this may occur was seen in Case 29. When examined originally there were definite signs of the disease with moderate disability but the patient survived until 1942. Though incontinent and inclined to be moody and sensitive, making her difficult to handle, she was able to walk with the aid of a stick until fourteen days before her death, when, without warning, she passed into a coma and died after a few days. Acute pyelitis and hyperpyrexia were terminal features in only 1 case and in 2 others the end was heralded by status epilepticus, epileptiform convulsions having occurred frequently during the preceding months. The most common determining cause of death in these cases was pulmonary, i.e. acute broncho or lobar pneumonia or acute bronchitis, these complications being usually accompanied by signs of cardiac failure. Cardiac failure alone was sited in 2 instances, 1 case being a man of 68. Toxæmia from septic bedsores was recorded in one instance. 2 cases, 12 and 37, died from malignant disease unconnected with their complaint. The former, though moderately disabled in 1929, showed little further progress in her malady and was able to continue at her work as a school teacher until 1941 when

she developed carcinoma of the colon with secondaries in the liver verified at operation. Case 37 would probably also have survived for a much longer period if it had not been for the development of a carcinoma of the uterus in 1939 which brought about her death. Case 23 is of interest for though severely disabled in 1929, she continued in this state in reasonably good health until 1935 when she was found to have a large right ovarian cyst. Incontinence was severe and it was thought that its removal might benefit this symptom. Though the operation was unaccompanied by any untoward incident she died suddenly and unexpectedly forty-eight hours later. Only one death was directly due to an accident (Case 35). Whilst confined to bed in a severely disabled state and attempting to light a cigarette she set the bedclothes on fire and died some days later as a result of toxæmia from extensive burns.

The Survivors

Clinical details of the 12 surviving cases are given in an appendix. In 1929, 8 of these had established signs of the disease and 4 showed little or no disability, the symptoms being suggestive of the disease in its early stages. Among the latter, Case 4 had an illness in 1933 in which the signs suggested scattered lesions but he has remained well since then. Case 30 had acute retrobulbar neuritis first in one eye, then after an interval in the other eye. The correctness of the original diagnosis may be questioned in these cases but there can be little doubt about the other 2. Case 13 began with acute retrobulbar neuritis and within a year developed right-sided hemiparesis. Case 31 is a woman who had transitory diplopia followed within a year or so by sensory disturbances in the lower limbs and ataxia. Re-examination this year failed to disclose any evidence of the former hemiparesis in the first case and was quite negative in the second where the only complaint was that when the patient walked far she noticed the right leg dragged. Such long remissions are of course not uncommon, especially after acute retrobulbar neuritis as Adie has shown (1929). But in Case 13, where motor signs followed so soon after retrobulbar neuritis, one was quite prepared, on the basis of personal experience, to find either the patient dead or severely disabled.

Table VII shows the cases grouped according to the extent of their original disability. It will be seen that little change has occurred during the interval except in the two instances underlined where the disease has progressed to severe disablement.

Table VII.—Progress of Disability in 12 Survivors

Extent of disability	1929 *cases*	1949 *cases*
None or slight ..	4, 13, 30, 31	4, 13, 30, 31
Moderate	14, 16, 17, 24, 36, 40	17, 24, 36, 40
Severe	1, 21	1, 14, 16, 21

Type of onset and survival.—This material is too small to draw conclu-

sions but study of the different modes of onset among the survivors shows that in the majority a complete remission followed and that there was no initial persistent disability (Cases 1, 4, 13, 14, 21, 24, 30, 31). Cases 36 and 40, however, are in striking contrast. The former took ill in 1927 with severe spastic paraplegia, cerebellar and brain-stem signs. It was nine months before he began to improve. In 1929 there was residual paraparesis which accounted for most of his disability, the other signs not being very pronounced. Since then he has remained in much the same state until two years ago when he began to complain of intractable trigeminal neuralgia of the same kind as has been described by Harris (1927), Parker (1928) and others. Case 40 also had severe initial symptoms with persistent disablement indicative of scattered lesions chiefly affecting cerebellar function. These signs are still present but he has had no further relapses and has improved to such an extent that for some years past he has been carrying on his full duties as a ploughman in charge of horses. It appears, therefore, that though the mode of onset may determine the extent of the initial disability – small or single lesions tending to cause symptoms which recover rapidly, and larger lesions symptoms which persist – a severe initial lesion is not incompatible with long survival.

Repeating character of symptoms.—A point to which little attention has been given in the literature is the way in which the same symptoms may recur in subsequent relapses. Often these remit completely but usually, after one recurrence, some permanent disability results. One is reminded of the course of events in peptic ulcer, another chronic disease which is characterized by remissions and relapses. It is the partly healed scar of an old ulcer crater that is the favourite site for a new lesion to form. As can be seen from Table I this repetitive feature in the symptomatology was present in many of the cases now dead. It was noticed also in 5 of the survivors. In Case 1, for example, there was transient paraplegia at 22 and recurrences at the ages of 43 and 46 respectively. In No. 16 the onset was by weakness in the left leg. An exacerbation of the same symptom occurred seven years later and there had been no other signs in the interval. Recurring motor weakness in the lower limbs was also a feature in Case 21, ataxia in 24 and acute retrobulbar neuritis in 30. With regard to this last symptom, the curious lack of correlation between the appearance of the optic discs after retrobulbar neuritis and visual acuity was remarked in several instances. Whether transitory blindness occurred early as in Cases 13, 30 or late as in 24 (thirty-one years after the onset) vision was rarely seriously affected and yet ophthalmoscopic examination revealed apparently a severe degree of primary optic atrophy.

Apparent arrest of the disease.—This was described by Taylor (1926) in several cases with one instance of complete recovery but as the period of observation was short it is not known what happened to the patients subsequently. Only two of the survivors in this series show signs of rapid

progression in their condition over the past twenty years. No. 16 is now hopelessly demented, bedridden and incontinent. Nothing is known as to what has determined his decline. In Case 14 where the disability has also progressed considerably, both childbirth and a surgical operation were related temporally to worsening of the clinical state. It is noteworthy, however, with regard to the much disputed question of the importance of childbirth that her first child was born without incident. It was the second pregnancy that was associated with the onset of symptoms (ataxia) and the third which was related to further deterioration in her condition.

The 4 " early " cases in 1929 which have already been referred to have shown no sign of fresh activity and the remaining 6 cases among the survivors with moderate or severe disability are much in the same state as when they were first seen. Case 17, a nullipara, is still able to do her housework thirty-one years after the onset of the disease. Though moderately disabled by spastic paraplegia she shows no sign of intellectual impairment or increased emotional lability and the sphincters are controlled though previously at one time she had had incontinence. Case 24 also shows the same good preservation of these functions. He looks after his shop and gets about with the aid of sticks. His illness began thirty-nine years ago and at first was remitting in character. He might have had no more relapses after 1929 had he not developed acute appendicitis in 1941 which led to an appreciable increase in his motor disability and to temporary blindness. Cases 36 and 40 have already been mentioned when describing the types of onset. In all these cases there appears to have been advance of the disease at first but in the past twenty-one years their condition has remained relatively stationary. This suggests that either their disease has been arrested or that some self-limiting process is at work. With the experience of Case 24, who kept stationary for years until he developed acute appendicitis, and of Case 36 who has in the past two years been suffering from trigeminal neuralgia, one would hesitate to accept the idea that the disease has been arrested. The frequency indeed with which trauma, and surgical operations, after years of apparent quiescence, lead to fresh exacerbation of the symptoms is at once a warning and at the same time an indication of the continued activity of the disease. It may be that it is the factor of personal resistance which is of chief importance in prognosis. It is remarkable too in many of the survivors that the disease has caused so little disturbance of intellectual, emotional and sphincter function.

Summary

A series of 40 unselected patients with disseminated sclerosis, all of whom lived in the same district and were seen twenty years ago, has been reviewed; 28 have died and 12 or 30 per cent survive.

(2) The average duration of the disease among the 28 dead patients was approximately twenty years ; when the whole series has died, this

average will naturally be still greater and the inclusion of the survivors at present indicates that the average for the whole series will be somewhat greater than twenty-two years. About 40 per cent of those now dead lived over twenty years. Possible explanations of this apparently high average have been discussed and it seems probable that it may be due to the natural survival period in the disease being much longer than has hitherto been supposed. Longevity in patients that survived longer than their fellows was usually only purchased at the expense of years of severe disablement. In the majority of those observed half the total illness was spent in this way.

(3) Coma often occurred as a terminal event in severely disabled patients and was sometimes preceded by frequent recurring epileptiform fits. Acute pulmonary complications, sepsis from bedsores and toxæmia from pyelitis are among the most frequent determining causes of death.

(4) Experience with these cases supports the general view that initial recovery of function usually follows a mild type of onset and that with more severe symptoms only partial recovery of function is likely to occur. Many patients, however, with severe initial symptoms have survived long periods though there has been some persistent disability from the onset.

(5) The tendency for symptoms to be repeated in subsequent relapses is observed as also the curious dissociation that exists between ophthalmoscopic appearances and visual acuity after acute retrobulbar neuritis.

(6) The almost stationary clinical condition exhibited by many of the survivors suggests that some self-limiting or defensive process is at work. It is considered unlikely that in these cases the disease is no longer active.

(7) Among the survivors there is relatively little evidence of gross sphincter disturbance, loss of emotional control or intellectual impairment. The preservation of these functions may be an important factor in the prognosis.

In the follow-up of these patients I am especially grateful to Miss S. V. Cooke, almoner to the Neurological Department of the Royal Victoria Hospital, Belfast, who undertook the main work of the enquiry. I am indebted to the medical practitioners in charge of many of the cases and to the Red Cross Society; Miss Wyatt, Director of Civilian Welfare, London, through whose co-operation it was possible to get into touch with many patients who would otherwise not have been traced. To Dr. E. A. Cheeseman of the Department of Social and Preventive Medicine, The Queen's University, Belfast, acknowledgment is also due for his valuable advice.

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APPENDIX

HISTORIES AND RESULTS OF CLINICAL EXAMINATION IN SURVIVORS

Case 1.—Female aged 75. The history obtained in 1929 was that in 1899, when the patient was aged 25, a febrile illness developed which was thought to be influenza. She became paralysed in the lower limbs and was confined to bed for three to four weeks. At that time she said she felt depressed and " imagined things." The weakness, however, disappeared and she remained symptom free until 1917 when she was aged 43. In January of that year she became emotionally upset for no apparent reason and noticed that the right arm and hand shook when she tried to use it. The symptoms passed off but in March of the same year, following a slight electric shock received whilst changing a light fixture, she noticed the right leg weak and numb and within two days was paraplegic. She made a good recovery after four months and kept well until 1920 aged 46, when weakness in the lower limbs recurred and persisted. In 1925 aged 51, she became ataxic and for some months was troubled with root pains in the right arm. In 1928, aged 54, she went blind in the left eye and was found to have acute retrobulbar neuritis. This recovered and when she was seen in 1929 she had had no further symptoms.

On examination 1929 she was confined to bed and was found to have a spastic paraplegia with bilateral Babinski sign and absent abdominal reflexes. There was sustained ankle clonus on either side and she could not stand without support. There was relatively good voluntary muscular power in the upper limbs but this was marred by gross intention tremor especially on the left side. There were no objective sensory disturbances and the sphincters were under control. Examination of the cranial nerves was negative. The mental state was exceptionally clear

and there was no increased emotional lability though the patient was cheerful and optimistic in her outlook. (W.R. and C.S.F. had been examined some years previously with negative results.)

In 1949 aged 75, the mental state is quite unaltered. Confined to bed since 1930 and without any voluntary movement in the spastic extended legs or in the left arm, she has a telephone by her bedside which she can use with the unimpeded right hand and so conduct her business. Vision is R. 6/9 and L. 6/12 with glasses. The discs are normal. There is a slight right ptosis which has been present for some years with some right divergent strabismus which varies from week to week. There is no nystagmus and the speech is unaffected. Vibration sense is entirely lost below the anterior iliac crests and light touch sensibility is impaired over the lower limbs but she still exercises good control over the sphincters and is not bothered in this way. It is thirty-two years since 1917 which is considered to be the year of onset but this may well have occurred fifty years ago, in 1899.

Case 4.—An ex-mental hospital male nurse, in 1923, when aged 33, developed " neuritis " in the right arm which lasted for some weeks. This was followed by severe occipital headaches. He found himself weeping without cause and his arms shook when he attempted to use them. The speech was dysarthric. At this time though the tendon reflexes were increased the plantar reflexes remained normal and there was no change in the cerebrospinal fluid. He was diagnosed disseminated sclerosis in the Liverpool Royal Infirmary where he was treated with arsenic under the care of the late Dr. John Owen. After about eight months he made a full recovery and had no further symptoms. In 1929 when he was first seen there was still some intention tremor of the right upper limb but this was not marked. In other respects examination was negative. The same is true to-day and the patient now aged 60 has no complaints and does full work. It is twenty-six years since his original illness.

Case 13.—Is a handyman who mends boots and works for builders as a plasterer in a village. In August 1929, when aged 25, he noticed aching pain in the right eye and in three days had become blind in the right eye. Vision was reduced to bare perception of light and there was some papillitis. The left eye was normal. W.R. negative. Within two months V.A.R. recovered to 6/9 and the disc showed pallor. At that time examination was negative save for loss of the right abdominal reflexes. He kept well until the spring of 1930, about nine months later, when he developed, over a period of a week, spastic hemiparesis involving the right side. He walked with a limp and was off work but after some months began to improve and the power returned to normal.

When seen in 1949, twenty years from the onset of symptoms, he was aged 46. He had had no further symptoms in the interval and is engaged in full work. On examination the pallor of the temporal half of the right disc was noted and V.A.R. was 6/12, V.A.L. 6/6. The abdominal reflexes were absent in all four quadrants but apart from these findings there were no other abnormal signs in the nervous system.

Case 14.—A female, had married at the age of 19. Her first child was born a year later without incident. At 24 she gave birth to a second child and it was during the puerperium that the disease first caused recognizable symptoms—ataxia of gait and emotional instability with laughing and crying which were attributed to hysteria, especially as she recovered fully within two to three months. She kept well for four years and then, following the birth of a third child vision was blurred, the speech became indistinct and there was weakness of the left leg and arm with gross intention tremor of the left arm and hand. Examined at this time in 1929, when she was aged 28, there was coarse nystagmus on looking to either side but particularly well marked to the right. There was marked dysarthria and a left-sided hemiparesis with increased tendon-jerks on this side and bilateral extensor plantar reflexes. The sphincters were controlled. Euphoria was very conspicuous

with excessive laughter and jocularity but memory and other intellectual functions appeared to be unimpaired. She could walk fairly well though she dragged the left leg.

In 1949 she was aged 48 and had had the disease for twenty-four years. She said she had improved after 1929 and had been able to do her housework and get about a little until 1940 when she was admitted to hospital to have an operation for hæmorrhoids. This substantially increased the disability so that she has not walked since and only gets out of doors by means of a wheeled chair. She has had no more children. On examination memory and intellectual functions appeared to be unimpaired. Though still euphoric with a constant cheerful mood she was restrained and sober in her talk and mood. The right optic disc looked pale and vision was 6/20 R. and L. Monocular nystagmus was seen on looking to either side. There was good power in the upper limbs and little or no evidence of the former ataxia. As regards the lower limbs both are weak but the left leg is now stronger than the right. Vibration sense was absent over the shins. No disturbance of sphincters. The tendon reflexes were generally increased, the abdominals absent and the plantars extensor.

Case 16.—This patient, a quarryman, had had his first symptoms in 1912 when he was aged 27. Following a minor injury he developed weakness of the left leg which remained severe for some months and then improved though it never entirely disappeared. Seven years later in 1919 the spastic weakness in the left leg grew worse again and he had difficulty in passing urine and some hesitancy in the flow. In 1929 the optic discs were normal, vision was unimpaired. There was no nystagmus and the functions of the other cranial nerves were normal. Some ataxia with intention tremor was observed in the right upper limb with spastic paresis of the left leg. The right leg was normal but he complained of cramps in both legs. Romberg's sign was negative and there were no sensory changes save an ill-defined band of hyperæsthesia at 2-3 L.V. The plantar reflexes were flexor but ankle clonus was present on both sides and there was general hyper-reflexia with absence of all the abdominal reflexes. There was disturbance of sphincter control as mentioned above.

In 1949, thirty-seven years after the onset of his illness he was found hopelessly incapacitated, confined to bed with incontinence of urine, spastic paraplegia in extension, double optic atrophy, defective vision and a presenile dementia. The decline in his condition was said to have dated from ten years ago.

Case 17.—A widow and former domestic worker, first noticed symptoms in 1918 aged 31 following influenza—weakness and ataxia of the lower limbs especially the right. This slowly progressed for three years and then improved sufficiently to enable her to walk again without much difficulty. After that her condition remained stationary except that on one occasion some years previous to 1929 the vision had beeen defective for a short time so that she could not read print. This recovered but a year or so later she found difficulty in holding the urine. In 1929, however, when she was first seen, her condition had been fairly static for about five years. She was able to walk without help though not for any great distance. The discs were paler than normal. There was no nystagmus and the functions of the other cranial nerves were normal. Some ataxia with intention tremor was observed in both upper limbs with a right-sided hemiparesis, more marked in the leg than in the arm. Romberg's sign was negative and there were no sensory changes. The plantars were extensor, ankle clonus was present and there was general hyper-reflexia.

In 1949, aged 62, thirty-one years after the onset of her illness she could still walk short lengths and do all her own housework, cooking, etc. There was no sign of any intellectual impairment or emotional lability. Vision was 6/6 in either eye with glasses and the optic discs were as before. The other cranial nerve functions were normal. There was fair power in the upper limbs and no trace of ataxia though the reflexes were increased. In the lower limbs there was moderate spasticity with

paraparesis, double Babinski's sign but no sensory changes and the sphincters were under full control.

Case 21.—A spinster. Was often ailing and easily made tired from the age of 21 onwards but it was not until 1916 when she was aged 25 that she noticed something wrong with the left leg. It felt " numb as if asleep " and also weak so that she was afraid of falling and walked with a limp. At that time she thought there was definite sensory loss to pin-prick below the level of the breast for she remembers the doctor commenting on it. She recovered after some months but between 1916 and 1919 the same symptoms recurred more than once, each time recovering. Since 1918 the weakness in the left leg persisted and between that time and 1929 she developed gradual increasing weakness in both legs with occasional precipitancy of micturition. In 1922 she recalls seeing double for a fortnight.

When examined in 1929 intellectual functions of memory and grasp were unimpaired. She was euphoric but not emotionally unstable. The optic discs were paler than normal but V.A. was 6/6 in either eye. There was no nystagmus or other signs of cranial nerve dysfunction. There was spastic paraplegia in extension, the patient being unable to stand without support and no voluntary movements of flexion being possible in the lower limbs. Spasticity was considerable but sensation was unimpaired. Babinski's sign was present, the abdominal reflexes being absent. In the upper limbs there was good voluntary power though the right hand grip was weak and tone increased on this side. There was slight intention tremor R.> L. with the finger-nose test. Though precipitancy of micturition occurred on occasions, on the whole there was fairly good sphincter control.

In 1949 vision was found to have deteriorated to approximately 6/60 in either eye and the discs were pale and atrophic. Memory was faulty, euphoria was conspicuous and there was increased emotional lability. There was still fairly full control of the sphincters and the only change in the paralysed state was that contractures had developed at the wrists and ankles with obvious wasting of the interosseal muscles of the hands and of the thenar eminences.

Case 24.—The proprietor of a village shop, aged 21, was cycling in December 1910 when his machine skidded on the ice-covered road and he was thrown into a pond of water. The next day and subsequently for some months he complained of a " tight band " round the stomach. It was suspected that he had injured his spine and he was X-rayed but with negative results. The late Sir Robert Jones ordered massage and the tight feeling gradually disappeared. In 1915, however, he began to find himself unsteady on his legs " staggering like a drunk man " so that for a time he had difficulty in keeping his balance. He recovered but the following year, in 1916, he noticed the right leg weak and stiff and for some months as on the previous occasion he walked with difficulty. Recovering again he kept well until 1920 when the spastic weakness in the right leg recurred together with ataxia of the right arm. This disability persisted until 1922 when both legs became paralysed and the right arm useless. He was confined to bed and treated in hospital, gradually recovering so that he was able to walk again with difficulty. When seen in 1929 there was coarse nystagmus on looking to either side especially the right. The optic discs were normal and no other abnormalities were found in the cranial nerves. The upper limbs appeared to be functioning normally though there was increase of tone on the left side and on the right weakness in the dorsiflexors of the ankle. The gait was spastic. Romberg's sign was negative and there were no objective sensory disturbances.

The patient is now aged 60 (1949) and it is thirty-nine years since he had the first symptoms or thirty-four years since he developed the ataxic gait. He was serving in his shop and managed to move about with considerable dexterity using a stick. Intellectually and emotionally he appeared normal. He said that from 1929 he had kept well but that in 1941 he had been taken ill with acute appendicitis and was six weeks in bed. This resulted in immediate worsening of his condition so that

he was unable to walk and had little use of the left arm. Vision was affected so that he could not read the newspaper. Gradually over a period of 2-3 years he improved and in the past 3-4 years his condition has been static again. On examination there was some pallor of the left disc with 6/12 vision as compared to 6/6 R. Coarse nystagmus was seen on looking to the right and on looking to the left he saw double (he had noticed this symptom for the past 2 months). In other respects the cranial nerves were normal. In the left upper limb there was a positive Hoffman's sign with marked increase of tendon reflexes on both sides. The left hand grip was weak and there was some intention tremor on this side with difficulty in performing rapidly alternating movements. Both plantars were extensor, the knee and ankle jerks were much increased. Vibration sense was lost over the shins, great toe-joint sensibility was absent and Romberg's sign was positive. The bladder and rectum function normally.

Case 30.—A single woman and a P.E. school teacher, aged 21 when in February 1927 she was affected with an acute retrobulbar neuritis of the right eye. Vision returned to normal in two to three months and she kept well until September 1928 (eighteen months) when she developed acute retrobulbar neuritis in the left eye. This time there was some associated papillitis but all investigations were negative as on the former occasion. She was first seen about this time but apart from the very brisk knee and ankle jerks no abnormalities were found in the nervous system.

When seen in 1949 she had been married some years and had a child aged six. No ill-effects had attended pregnancy or followed the confinement. She had had no further symptoms and there was no disability. Visual acuity was 6/9 with either eye in spite of the fact that the optic discs were generally pale, the lamina cribrosa being very apparent. Yet the pupillary reactions were brisk and the fields of vision on confrontation full. Neurological examination was otherwise negative.

Case 31.—A single woman aged 28 in 1929, developed diplopia for two months. No cause was found and the condition recovered spontaneously. Apart from absent lower abdominal reflexes there were no other signs. About one to one and a half years later she sustained a wetting and the next day on waking noticed numbness in the legs from the waist downwards with pins and needles in the feet. The bladder function was not disturbed and there was little muscular weakness though her gait was unsteady. After a holiday these symptoms which were persistent and disturbing for five to six weeks, gradually subsided.

When seen in 1949, aged 48, she was in good health and had no symptoms save that when she walked for any great distance the right leg was liable to drag and the toes catch on the ground. On examination there was no trace of any motor, sensory, or reflex abnormalities and the cranial nerve functions were normal.

Case 36.—A labourer first noticed weakness and paræsthesiæ in the left leg and then in the right in 1927 when he was aged 23. Walking became difficult and he was admitted to hospital where he showed nystagmus to the left, slow speech, intention tremor of the upper limbs, absence of the right abdominal reflexes, bilateral extensor plantar responses and much increased tendon reflexes with precipitancy of micturition. C.S.F. was negative save for the colloidal gold test : 0123332 100. He felt worse after return from hospital but after some months began to improve. On examination in 1929 the nystagmus had disappeared and speech was normal. There was no ataxia or other signs of motor abnormality in the upper limbs but the right leg was spastic and tired readily. Romberg negative. No sensory signs. Some difficulty in starting flow of urine. Plantars extensor.

In 1949, twenty-two years from the onset of symptoms, aged 45, he had still fairly good use of the legs and was able to walk moderate distances without assistance, the motor and reflex signs being the same as those noted twenty years previously. No fresh symptoms had occurred in the interval and to all intents and purposes his condition was static. Vibration sense was diminished over the left shin and lost over the left great toe. The left arm was spastic and showed some

dysdiadokokinesia. He had full control of his sphincters. Intellectually and emotionally he would pass for normal. His only complaint was a persistent right-sided trigeminal neuralgia which had followed the extraction of a tooth two years ago.

Case 40.—A ploughman was 26 in 1924 when he noticed the gait ataxic as if he were drunk. If he looked up suddenly he had to grasp hold of something quickly to prevent himself falling. Later in the same year he noticed stiffness and weakness of the left leg. Soon he was unable to walk unaided and in 1925 he was admitted to hospital where he remained ten weeks. At that time he had bilateral extensor plantar reflexes, absence of the right abdominal reflexes, general hyper-reflexia, dysarthria and partial blindness. He was treated by N.A.B. but for some months was worse rather than better. After some months, in 1926, he began to improve and to walk again, the other symptoms having remitted. When seen in 1929 he showed no intellectual or emotional change, vision was normal and the discs appeared to be healthy. There was coarse nystagmus on looking to the left. Speech was normal. Slight terminal intention tremor was present with the finger-nose test on the left side but apart from this there was no other evidence of ataxia or other motor disorder in the upper limbs. Romberg sign was negative and apart from decrease of vibration sense in the left leg there were no other sensory signs. The gait, however, was inclined to be ataxic and reeling in character. Plantars were both flexor and the abdominals were present. Tendon reflexes all increased. Sphincters controlled.

In 1949, twenty-five years after the onset of symptoms this man is still doing a full day's work in the fields as a ploughman. He can walk any reasonable distance and has been aware of no symptoms in the past twenty years save an occasional fall through being unsteady on his feet. Vision was R. 6/9 and L. 6/12 with glasses. The right disc was possibly a little pale. There was paralysis of both internal recti noticeable on attempts at convergence and when looking to the sides. This was associated with monocular (ipsilateral) nystagmus on looking to the right or to the left. Voluntary muscular power is strong in both arms and apart from some difficulty in performing rapidly alternating movements with the right hand there is no motor abnormality. The gait is ataxic, cerebellar in type and Romberg's sign is positive though there are no definite sensory changes in the lower limbs. Right plantar doubtful extensor, left flexor. Abdominal reflexes absent, except in right lower quadrant. Knee and ankle jerks increased but there is little alteration in muscular tone. Sphincters controlled.

Notices of Recent Publications

Observations on the Pathology of Hydrocephalus. By Dorothy S. Russell. M.R.C. Special Report Series No. 265. 1949. Pp. 138 with 90 illustrations. London : H. M. Stationery Office. Price 6s. net.

The material on which this monograph is based has been collected by the author during the past seventeen years, chiefly at the London Hospital. It appears to comprise cases of every known ætiology, and while secondary hydrocephalus due to tumours or meningeal adhesions forms a large proportion of the material, many cases of the more interesting "primary" or congenital forms have also been examined. The monograph forms a very complete survey of the ætiology and pathology of ventricular dilatation. There may be criticisms of the author's views on certain developmental problems, but most of her conclusions will receive common assent.

The most interesting chapter is that dealing with the maldevelopments causing or associated with hydrocephalus. These may occur in the aqueduct of Sylvius, the foramen of Magendie, the base of the skull or the lumbo-sacral spine and spinal cord. Obstructions at the level of the aqueduct are divided into stenosis and " forking of the aqueduct, and the formation of septa across it, all of which are considered to be malformations, and gliosis of the aqueduct, which, although its cause is unknown, seems to come on after birth. *Stenosis* appears to be a rare condition in which the hydrocephalus, though dating from birth, need not be severe or progressive. In the more common " forking " a narrow central slit is associated with one or more small rounded channels ; all of these are lined by ependyma and groups of misplaced ependymal cells are often seen in the neighbourhood. *Septum formation* is also not very uncommon. The septum usually bridges the aqueduct at or near its lower end. *Gliosis* of the aqueduct must be distinguished from slowly growing astrocytomas of the quadrigeminal plate. In this form there is evidence of progressive stenosis by overgrowth of the subependymal neuroglia and the original outline of the aqueduct is still seen as an irregular line of ependymal cells or a line at which the gliosis begins. The wall of the narrowed aqueduct may or may not be lined by ependyma, indeed there is a great variation, in this form, in the character of the aqueduct and its surroundings. This lesion may be part of a widespread ependymitis or may be due to a locally acting cause, the nature of which is quite unknown.

In an otherwise excellent description of the Arnold-Chiari malformation the author gives little importance to cases in the adult. She has never found the deformity associated with spina bifida occulta alone, but always with meningo-myelocele, or at least meningocele. Her observations do not support the common view that the deformity is due to traction on the medulla resulting from fixation of the spinal cord to the spine at the level of the spina bifida. Rather she is inclined to the theory of Schwalbe and Gredig, which dates the origin of the deformity to an early stage of embryonic development.

The relation of hydrocephalus to birth trauma, especially to subarachnoid hæmorrhage and to thrombosis of venous sinuses is fully discussed. That hydrocephalus may result from subarachnoid hæmorrhage has been experimentally confirmed, but tying venous sinuses in animals has almost always failed to produce it. There are, however, many clinical cases in which thrombosis, especially of the sagittal sinus, has been associated with dilatation of the ventricles.

The final chapter on the anatomical effects of hydrocephalus contains much that is of interest to the clinician as well as to the pathologist. Damage to the hypothalamic nuclei may lead to precocious puberty on the one hand or to infantilism on the other. The secondary results of stretching on the walls of the ventricles are also described; rupture of the wall with formation of false diverticula, local ballooning of the walls, and replacement of ependyma by neuroglial hyperplasia. The two former may open the way to a freer absorption of cerebrospinal fluid and so to spontaneous relief of intracranial tension, although they may also cause permanent symptoms due to local destruction of brain tissue.

The author includes the report of 51 selected cases, and these, along with the excellent illustrations, help greatly in the elucidation of what is still a difficult subject. In spite of its modest title and price this is an authoritative and important work which no one interested in the neurology of childhood can afford to neglect.

Perspectives in Neuropsychiatry. Essays presented to Professor F. L. GOLLA by past pupils and associates, edited by D. RICHTER. 1950. Pp. 229. London: H. K. Lewis. Price 15s.

Dr. Golla may be congratulated upon the deserved recognition represented by this collection of essays, and upon the affection he has so manifestly inspired in his fellow workers.

Of these fourteen essays, three only deal directly with psychiatry, the rest being devoted to anatomical and physiological problems. Of these some stand out by reason of their substance and lucidity and of the prudence and restraint of their conclusions. Others are not so happy, for their authors cherish the notion that the brain is an "engine," "mechanism" or "machine" which performs all the functions hitherto regarded as the prerogative of the intellect and takes abstract thinking easily in its stride. For them the mind is not an activity, it is a sort of machine that is sometimes working and sometimes idle, but is equally open to inspection in both circumstances.

It will be seen, then, that there is the widest possible diversity of philosophic background to these essays, and some of them have no metaphysical presuppositions whatever. These are the ones that most confidently promise the impending solution of all those problems that have defeated the acutest of human intellects since the time of Plato. Thus, for Dr. Brazier in her essay on neural nets and the integration of behaviour, the final revelation that man is just a "servo-mechanism" is only round the corner, as a result of the work of Pitts and McCulloch, and religion, politics, law and social science are about to be revolutionized by the concepts of "feed-back" mechanisms and reverberating circuits. These notions may be new, but the philosophical fallacy of anti-intellectualism is not, and here it stands before us ineffectually disguised in the dowdiest of "new looks."

In a comparably confident frame of mind, Dr. Hutton, dealing with the relationship of mind and matter to personality, complains that hitherto all philosophers have neglected the part played by the body in our perception of the external world. But surely she should know that for over twenty years this problem has figured prominently in Whitehead's philosophy and has been expounded at length in many of his writings.

The contributor who moves with greatest ease on this difficult terrain is Dr. Russell Brain in his interesting discussion of the concept of the schema in neurology and psychiatry. What William James has called "a belated drinker at the Kantian stream," he traces its derivation from Kant and seeks to apply it to the speech function. It is probable, however, that a fruitful conception of speech cannot be built upon the notion of the "word" as the operative element. Hughlings Jackson reminded us that the unit of referential speech is the proposition, and not the

" word " (or the "name" to be more correct). The English language has its univocal names, and Dr. Brain has chosen one of them, namely, " dog " as his example, but it has many equivocal " names," the meanings of which vary with the propositional contexts in which they are used, and to apply to them his concept of the schema is not so easy.

Let us take the simple name " chest," this has completely differing referents according as it is used by a medical man, a member of the Hebdomadal Council of Oxford University, or by Robert Louis Stevenson in " Treasure Island." Are we to suppose that the utterance of this sound always evokes the same uniform pattern of rhythmic excitation in the auditory cortex ? It has no discoverable meaning apart from its propositional context, and where and how does it acquire its appropriate symbolic value on any given occasion of its use ?

It seems that the application of the Kantian schema to " words " is comparable with the notion still held by some that " muscles " as such are " represented " in the motor cortex rather than movements, and to be an idea just as illusory, and inadequate to explain the facts of experience. Any attempt to use the schema for speech must surely start from the conception of the proposition as the unit of speech. This makes the problem infinitely more complex.

Of outstanding interest to neurologists are the essays on the hypothalamus by Professor Le Gros Clark, upon the anatomical lessons from prefrontal leucotomy by Professor Meyer, upon electro-encephalography as an instrument of research by Dr. Denis Hill, upon the endocrinology of mental disturbances by Drs. Hemphill and Reiss, and upon genetics in psychiatry by Dr. Eliot Slater. Dr. Grey Walter's contribution on the electrophysiology of mental mechanisms is less cautious and informative. He tells us that " with only a secondary school smattering of physics and physiology and a few simple rules, a recordist (of the EEG) can locate 80 per cent of intracranial lesions " and " can assist materially the diagnosis and prognosis of the majority of people who complain of seizures." Many of us who have been far more favoured in the attainments of our "recordists" and interpreters of the EEG have found ourselves very much less fortunate in the scorings achieved, and they will ask whether the author of this article has quite made up his mind whether he wishes to convey information, or to create an impression, and if the latter, what kind of impression ?

From the title of this collection of essays it may be surmised that there are some amongst psychiatrists who are turning away from their generation-long allegiance to the exotic symbolisms of modern psychological theory, and from the sacerdotalism that has been an integral element in them. Yet the pendulum may swing too far in the intoxication of a new-won freedom, and whether those who now turn so hastily from allegory to machinery are moving towards stability or merely being " carried about with every wind of doctrine " remains to be seen. Nevertheless, the change is an omen, but not yet a discernible promise that the age-old problem of the body-mind relationship is any nearer resolution. In some of these essays we meet yet again the old logical and philosophical fallacies and the old confusion of categories that have bedevilled this subject for centuries. Nothing cruder has yet been proposed than that man is merely a " servo-mechanism," inexplicably growing, reproducing, fuelling, decarbonizing and repairing himself. How true it is that " the only safe way to meet facts is to be well provided with ideas in good order."

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